# A STUDY OF" THE CORELLATION BETWEEN POTASSIUM DIP AND SEVERITY OF ACUTE ISCHEMIC STRESS IN PATIENTS WITH ACUTE CORONARY SYNDROME"

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**M.D. (GENERAL MEDICINE) - BRANCH – I**


**GOVERNMENT KILPAUK MEDICAL COLLEGE**

**CHENNAI**

**April – 2014**

## BONAFIDE CERTIFICATE

This is to certify that **"A STUDY OF THE CORELLATION BETWEEN POTASSIUM DIP AND SEVERITY OF ACUTE ISCHEMIC STRESS IN PATIENTS WITH ACUTE CORONARY SYNDROME"** is a bonafide work performed by **Dr .S.KATHIRAVAN**, post graduate student, Department of Internal Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in fulfilment of regulations of the Tamil Nadu Dr. M.G.R Medical university for the award of M.D. Degree Branch I (General Medicine) during the academic period from May 2011 to April 2014.

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# DECLARATION

I solemnly declare that this dissertation **"A STUDY OF THE CORELLATION BETWEEN POTASSIUM DIP AND SEVERITY OF ACUTE ISCHEMIC STRESS IN PATIENTS WITH ACUTE CORANARY SYNDROME"**was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Dr.D.SURENDRAN.**, Professor and Head of the Department of Internal Medicine, Government Kilpauk Medical College and Hospital, Chennai.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfilment of the University regulations for the award of the degree of **M.D. Branch I (General Medicine)**.

Place: Chennai

Date: (Dr. S.KATHIRAVAN)

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# ABSTRACT


## BACKGROUND AND OBJECTIVES

Coronary artery disease is the important cause of mortality and morbidity in the world as well in India.

Transient decrease in serum potassium during episode of acute coronary syndrome is thought to be a common finding, but so far there are not many studies demonstrating it occurrence in ACS and its significance. Delta potassium defined as the difference between potassium during the time of discharge and on admission [k-k at the time of discharge- k at the time of admission] reflect potassium drop during acute coronary syndrome and it has been thought to be associated with the disease severity in patient with ACS.

Apart from well-known factors influencing mortality and morbidity in patient with acute coronary syndrome like female sex, associated co morbid illness like diabetes mellitus[DM], Systemic hypertension[SHT], dyslipidaemia, age , smoking, alcoholism, delta potassium has also thought to be associated with disease severity and influence the course of the disease in patients with ACS.

The present study is an attempt to study its prevalence and its significance in patient of acute coronary syndrome group.

## METHODS AND MATERIALS:

**STUDY DESIGN:** CROSS SECTIONAL STUDY.

**STUDY GROUP: Patients with acute coronary syndrome**

**1] STEMI 2] UNSTABLE ANGINA 3] NSTEMI**

**MATERIALS:** Detailed history, Physical examination, ECG, 2D Echocardiography, Chest x-ray, Complete Haemogram, Rbs, Blood urea, Serum Creatinine, Serum potassium, cardiac enzyme CPK-MB, Urine Routine, Total Cholesterol, Triglyceride levels.

**PLACE OF STUDY:** Govt. Kilpauk medical college hospital

**DURATION OF STUDY:** 6 months

**METHODOLOGY:1)**Potassium dip will be assessed by Δk-potassium at the time of discharge – potassium at the time of admission.

2) Severity of ACS assessed by

a) Duration of hospital stay b) 2D echo c) Cardiac enzyme CPK-MB assay.

**INCLUSION CRITERIA:**

All patients > 35 yrs of age admitted with 1st episode of acute coronary syndrome,

**EXCLUSION CRITERIA:**

1] Previous history of CAD. 2] Patients with CKD. 3] Patients on potassium controlling agents like ACE inhibitors, diuretics etc.

## RESULTS

A] Among 65 patients with STEMI 47 had delta potassium value more than 0.5 which constitute 72%. In patients with NSTEMI 66% has significant delta potassium. But in UNSTABLE ANGINA group only 23% has delta potassium more than 0.5.

B] Delta potassium has also shown to be positively correlated with duration of stay in hospital as shown below.
1] Patient who stayed for 5 or less- 19% has significant delta potassium
2] In the patient who stayed for 5 to 7- 76% has delta potassium more than 0.5
3] In patients who stayed for more than 7 days- 96% has significant delta k.

C] The relationship between delta potassium and LV dysfunction also correlate positively. In 17 patients with normal only 2 has delta potassium more than 2. In patients with mild LV dysfunction 33% has significant delta potassium. But 92% of patients with moderate and 93% of patients with severe LV dysfunction has delta potassium more than 0.5.

## CONCLUSION

1] Prevalence of potassium dip is common among patients with acute coronary syndrome.
2] Diabetic patients does not have significant delta potassium.

3] Low potassium value at the time of admission [less than 4] was not found to correlate with disease severity in this study.
4] Delta potassium was positively correlated with severity of ischemic stress in patients with ACS.
5] Age, sex, diabetes, SHT, dyslipidaemia, smoking and alcoholism do not have major impact on delta potassium.


## KEY WORDS

1] Delta potassium 2] acute coronary syndrome 3] severity of ischemic stress 4] duration of stay5] left ventricular dysfunction.

# INTRODUCTION

Coronary artery disease is the important cause of mortality and morbidity in the world as well in India. Patient with ischemic heart disease falls in to two major group- stable angina and acute coronary syndrome[ACS]. Patient with acute coronary syndrome falls into three major group 1] patient with ST elevation myocardial infarction (STEMI), 2] NSTEMI(non ST elevation MI), 3] unstable angina. The prevalence of risk factors as well as IHD is increasing in developing countries like India.

Transient decrease in serum potassium during episode of acute coronary syndrome is thought to be a common finding, but so far there are not many studies demonstrating it occurrence in ACS and its significance. Delta potassium defined as the difference between potassium during the time of discharge and on admission [k-k at the time of discharge- k at the time of admission] reflect potassium drop during acute coronary syndrome and it has been thought to be associated with the disease severity in patient with ACS.

Apart from well-known factors influencing mortality and morbidity in patient with acute coronary syndrome like female sex, associated co morbid illness like diabetes mellitus[DM], Systemic hypertension[SHT], dyslipidaemia, age ,

smoking, alcoholism, delta potassium has also thought to be associated with disease severity and influence the course of the disease in patients with ACS.

The present study is an attempt to study its prevalence and its significance in patient of acute coronary syndrome group.

## AIM OF THE STUDY:

1) To study the prevalence of delta potassium in patient with acute coronary syndrome.
2) To study the distribution of delta potassium in various group of patient in acute coronary syndrome.
3) To study the correlation between delta potassium and disease severity in patients with acute coronary syndrome.

# REVIEW OF LITEREATURE

## EPIDEMIOLOGY OF CHDIN INDIA:

Coronary heart disease is emerging as the leading cause of death in India and also worldwide. Previously it was thought to be prevalent primarily in developed countries but it now leads to more death and morbidity in low and middle-income countries [ex: India] and rates are increasing disproportionately when compared to developed countries. It affects young people in low- and middle-income countries, when compared to high-income countries. Thus it has a greater impact on economic development in low- and middle-income countries [1].

## PREVALENCE OF CHD INDIA [2007 ESTIMATES]

FIG: 1 SHOWING URBAN PREVALENCE OF CHD.

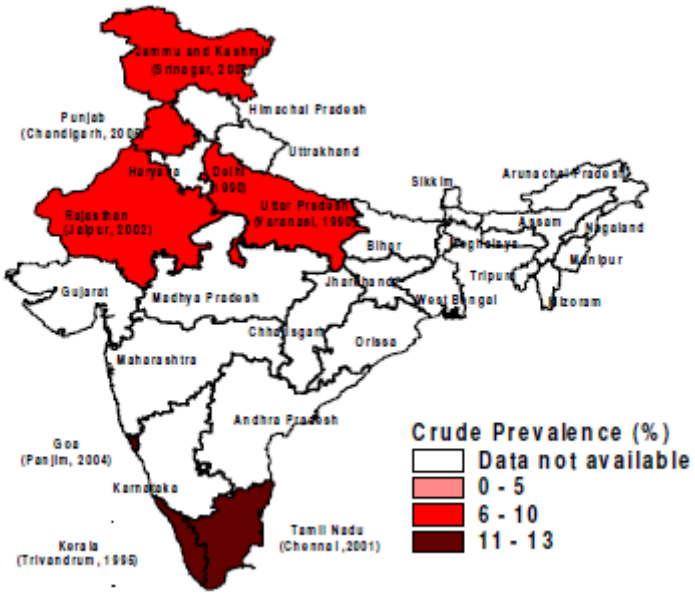
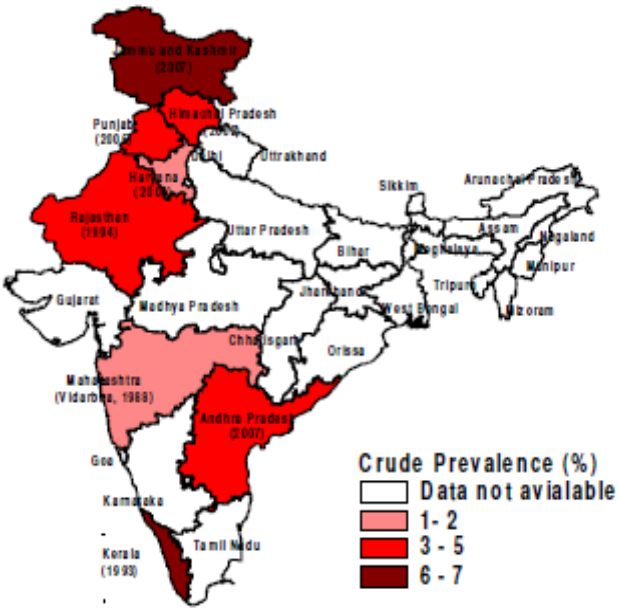


FIG:1. 2 SHOWING RURAL PREVALENCE OF CHD




## TABLE 1 SHOWING BURDEN OF CHD IN WORLD AND INDIA

Mortality Associated with CHD

*Global CHD Mortality*

In 2004, CHD was the leading cause of death worldwide, leading to:

- 7.2 million deaths (12.2% out of a total of 58.8 million deaths)
- 134.0 deaths per 100,000
- 138.6 age-standardized deaths per 100,000
- 22,370,000 DALYs (disability adjusted life-year)
- 222,762 age-adjusted DALYs per 100,000

*CHD Mortality in India*

In 2004, CHD was the leading cause of death in India, leading to:

- 1.46 million deaths (14% out of a total of 10.3 million deaths)
- 130.7 deaths per 100,000
- 207.7 age-standardized deaths per 100,000
- 15,588,000 DALYs
- 1,931 age-adjusted DALYs per 100,000

(WHO, 2004; WHO, 2009)

The above table is a comparison between India and world burden of coronary artery disease.

## ACUTE CORONARY SYNDROME:

Three groups of patients are included in acute coronary syndrome

1) STEMI

2) NSTEMI

3) UNSTABLE ANGINA.

UA is diagnosed when patient have chest pain or other similar symptoms or least any of the following one features:

(1) It comes even during rest (or only with minimal exercise) and last for prolonged period usually >10 minutes.

(2) Pain becomes severe and of recent onset (i.e., last four to six weeks).

(3) The pain increases in ascending pattern (i.e.it becomes more severe, last longer, occur more frequently than previously).

NSTEMI is diagnosed if the patient has the clinical features of unstable angina and evidence of myocardial necrosis, as evidenced by elevated cardiac enzymes. STEMI is diagnosed when patient with typical angina pain has ST elevation in 12 lead ECG and raised cardiac biomarkers.

## ATHEROSCLEROSIS

Atherosclerosis is characterized by the presence of intimal lesions called as **atheroma's**[also called atherosclerotic plaques] which protrude into affected vessel lumen[2]. The atheromatous plaque consists of a raised lesion with soft,yellow core which consist of lipid (mainly cholesterol and cholesterol esters) and covered by a firm, white fibrous cap. This cause obstruction to blood flow, and also weaken the underlying media and when it ruptures, causes acute catastrophic vessel thrombosis.

**TABLE.2.**RISK FACTORS FOR ATHEROSCLEROSIS

| Major Risks | Lesser, Uncertain, or Nonquantitated Risks |
|---|---|
| ***Nonmodifiable*** | Obsesity |
| Increasing age | Physical inactivity |
| Male gender | Stress ("type A personality) |
| Family history | Postmenopausal estrogen deficiency |
| Genetic abnormalities | High carbohydrate intake |
| | Lipoprotein(a) |
| ***Potentially Controllable*** | Hardened (trans)unsaturated fat intake |
| Hyperlipidemia | |
| Hypertension | *Chlamydia pneumoniae infection* |
| Cigarette smoking | |
| Diabetes | |
| C-reactive protein | |

## NON MODIFIABLE RISK FACTORS

### Age

Age has a dominant influence in atherosclerosis pathogenesis. Though the accumulation of atherosclerotic plaque is a progressive process, it does not clinically manifest until lesions reach a critical threshold. Then it begins to cause organ injury in middle age or later. Thus, in fourth to sixth decades of ages, the incidence of myocardial infarction in men increases by five times [3] even though the underlying arterial lesions were evolving before that.

### Gender

Premenopausal women are protected against atherosclerosis and all its complications if compared to men of same ages. This explains why myocardial infarction and other complications of atherosclerosis are uncommon in premenopausal women unless they have other risk factors for MI like diabetes, hyperlipidemia, or systemic hypertension [4]. However, after menopausal age, the incidence of atherosclerosis-related diseases begins to increases and with advanced age eventually becomes more than that of men. This is explained by favourable influence of oestrogen on this process.

## GENETICS

The familial tendency to atherosclerosis and its complication Ischemic heart disease is a well-known fact and it is influenced by several factors. In some instances it is due to presence of other risk factors, such as systemic hypertension or diabetes in the same family whereas in others it involves well-defined genetic derangements in lipid metabolism, such as familial hypercholesterolemia, that result in excessively high blood lipid levels [5].

## MODIFIABLE RISK FACTORS

### Hyperlipidemia

It is a well-known major risk factor for atherosclerosis; even in the absence of other risk factors, hypercholesterolemia by itself can cause lesion development. The most important serum lipid component associated with coronary heart disease is low-density lipoprotein (LDL) cholesterol [6].LDL cholesterol major function is to deliver cholesterol to peripheral tissues. In contrast, high-density lipoprotein [HDL] mobilizes cholesterol from atheromas and transports it to the liver after which is excreted into the bile [7]. Hence higher levels of serum HDL is associated with reduced risk.

Diet and pharmacologic approaches which lower LDL or total serum cholesterol, and raise serum HDL are all of considerable interest. High dietary

intake of egg, animal fats and butter raises plasma cholesterol levels. On the other hand intake of diets low in cholesterol and with higher ratios of polyunsaturated fatty acids lowers plasma cholesterol levels. Omega-3 fatty acids (rich in fish oils) are beneficial, whereas unsaturated fats which are produced by hydrogenation of polyunsaturated oils (present in baked foods and margarine) negatively affect cholesterol profiles. Regular exercise and moderate intake of alcohol raise HDL levels, whereas obesity and smoking decreases it.

**HYPERTENSION**

Hypertension is another major important risk factor which is associated atherosclerosis; systolic and diastolic blood pressures are equally important. Ischemic heart disease risk increases by approximately60% in hypertensive patients when compared to populations with normal blood pressure [8]. When hypertensive patient is not treated approximately half of patients will die of IHD or congestive heart failure, and another third will die with the development of stroke.

**CIGARETTE SMOKING**

Cigarette smoking is associated with increased risk in men, and women. Chronic daily smoking of more than one pack of cigarettes increases the death rate from IHD by 200%. When it is stopped the risk is reduced markedly

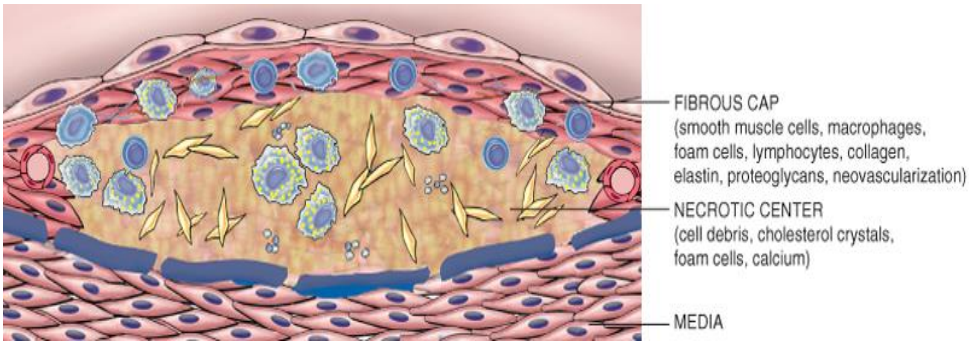
**DIABETES MELLITUS**

Diabetes aggravates dyslipidaemia and atherosclerosis occurs more frequently. The risk of acquiring MI is twice in diabetes as compared to non-diabetes.

## PATHOGENESIS

The atherosclerosis is a chronic inflammatory process of the arterial wall which occurs following endothelial injury [9].Lipoproteins, lymphocytes, macrophages and the normal cellular constituents of the arterial wall all interacts and it lead to the progression of the atherosclerosis lesion. The proposed hypothesis is endothelial dysfunction results from chronic endothelial injury and result in high permeability, leukocyte adhesion, and accumulation of lipoproteins (mainly LDL and its oxidized forms) in the vessel wall, after adhesion to the endothelium monocytes migrates into the intima and it is converted into macrophages and foam cells [10]. Platelet adhesion Factor gets released from activated platelets, and vascular wall cells and it induces SMC recruitment, either from the tunica media or from circulating precursors. Lipid accumulation occurs both outside the cells and intracellularly.

**FIGURE 1.3 SHOWING ATHEROMA COMPONENTS**



## CORONARY ATHEROSCLEROSIS:

Atherosclerotic disease occurs mainly in large vessel like epicardial coronary artery. The important factors associated with atherosclerosis (increased plasma LDL , decreased serum high-density lipoprotein , chronic smoking, hypertension, and DM) interferes with the normal functions of the vascular endothelium which include control of local vessel tone, maintaining antithrombotic surface, and control of inflammatory cell adhesion and diapedesis. When these properties are lost it results in pathologic constriction, thrombus formation, and abnormal interactions among blood cells, most importantly between macrophages and platelets and the activated vascular endothelial cells. These functional changes lead to the subintimal collections of lipids, smooth muscle cells, fibroblasts, and intercellular matrix that result in the atheroma formation. There is a tendency for atherosclerotic plaques to form at sites where increased turbulent coronary flow occurs, commonly at branch points in the epicardial arteries. When vascular stenosis reduces the diameter of an epicardial artery by 50%, ability to increase coronary flow is limited when myocardial demand is increased. When the diameter is reduced by approximately 80%, blood flow may be reduced even during period of rest, and further small decreases in the stenotic orifice area can decrease coronary flow markedly and cause myocardial ischemia at rest or only with minimal stress [11].

Narrowing of epicardial coronary artery by atherosclerosis in most of case is caused by the formation of a plaque, which can leads to rupture or erosion of the cap and this separates plaque from the bloodstream. When plaque contents is exposed two important and related processes occurs: (a) platelets activation and aggregation, and (b) the coagulation process is activated, which results in deposition of fibrin strands [12]. The thrombus consist mainly platelet aggregates and fibrin strands along with red blood cells and it can reduce coronary blood flow, resulting in the clinical manifestations of myocardial ischemia.

The location of the thrombus determines the quantity of myocardial cells becoming ischemic and determines the severity of the clinical features. Thus, critical obstructions narrowing diameter of coronary vessels, such as the left main coronary artery and the proximal portion left anterior descending coronary artery, are associated with poor outcome. Chronic severe coronary vessel narrowing and myocardial ischemia ultimately result in the development of collateral blood vessels, particularly when the narrowing develops gradually. When well developed, such collateral vessels alone can provide sufficient blood flow and sustain the viability of the myocardial cells at rest but not during time of increased demand [13-16].

## PATHOPHYSIOLOGY

UA/NSTEMI is caused by a reduction in oxygen supply or by an increase in myocardial oxygen demand which is superimposed on a lesion that causes coronary arterial obstruction, usually an athero thrombotic coronary plaque.

Pathophysiologic processes that are involved in the development of UA/NSTEMI can be explained as follows [17-20]:

(a) Plaque rupture or erosion which leads to formation of superimposed non occlusive thrombus in such patients, NSTEMI will occur when platelet aggregates and/or atherosclerotic debris embolise to vessels which are further down.

(b) Transient vessel wall narrowing [e.g., coronary vasospasm in Prinzmetal angina]

(c) Progressive occlusion of vessel (e.g., rapidly developing coronary atherosclerosis or stenosis of coronary vessel after coronary intervention)

(d) UA in due to increased myocardial oxygen requirements and decreased blood supply.

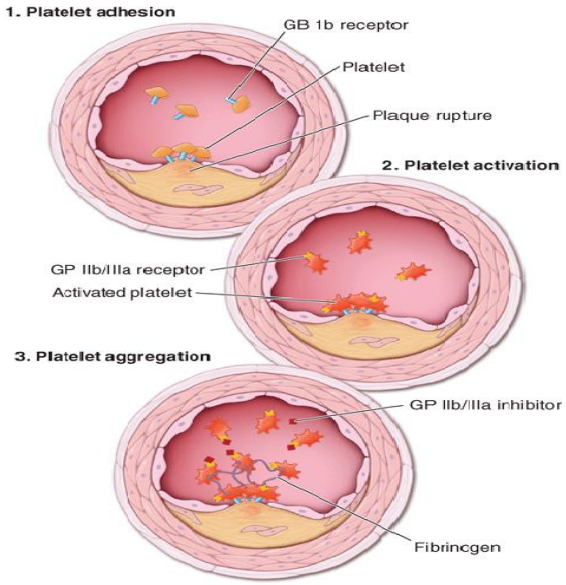
More than one of the above said process may be involved in the same patient.

5% of the patients with unstable angina or non ST elevation MI when studied angiographically have stenosis of the left main coronary artery, fifteen percent

of patients have triple vessel CAD, thirty percent have disease in two coronary vessel, forty percent disease in one coronary artery, and ten percent have no significant epicardial coronary vessel stenosis, in this group the pain may be due to obstruction in coronary microcirculation. Narrow neck and stenosis in the eccentric region are the angiographic finding of the pathologic atheromas lesion [ 21-22].

Angioscopy has been reported to show "white" thrombus, which is rich in platelet in contrast to "red" thrombus which is rich in fibrin and cells; the latter are very often seen in patients with acute ST elevation myocardial infarction. Most of these patients with UA/NSTEMI have multiple plaques which are at risk of disruption and are called as vulnerable plaques.

**FIG 1.4*PROCESS OF THROMBUS FORMATION INVOLVING PLATELET ADHESION, ACTIVATION AND AGGREGATION***



# CLINICAL PRESENTATION

## History and clinical features

pain in the left retrosternal or discomfort in the epigastric region are the most common presenting feature in patient with acute coronary syndrome, and frequently radiates to the region of neck, left shoulder but more commonly to the left arm. This discomfort is usually very severe and may be experienced as frank pain [23].

“Anginal equivalents" are features other than chest pain in patients with CAD such as breathlessness and discomfort in epigastric region may also occur, and these occurs frequently in females [24].The physical examination is similar to that seen in patients with stable angina and sometimes not well prominent. If the patient is affected by severe myocardial ischemia or extensive NSTEMI, the clinical features like increased sweating, pale and cool peripheries, increased heart rate, gallop rhythm, pulmonary creps and shock, similar to the features seen in patients with STEMI can be seen [25].

Evaluation of patients with suspected unstable angina/NSTEMI should include the expert opinion of whether the chest discomfort likelihood of being caused by [26] myocardial ischemia can be in one of three categories: high, intermediate, or low.

## TABLE 3: SHOWS PROBABLITY OF CHEST PAIN BEING ANGINA.

| |
|---|
| **High Likelihood** |
| Known coronary disease (particularly recent percutaneous coronary intervention) |
| Typical angina reproducing prior documented angina |
| Hemodynamic or ECG changes during pain |
| Variant angina |
| ST-segment elevation or depression of at least 0.5 mm |
| Marked symmetric T-wave inversion in multiple precordial leads |
| Elevated cardiac enzymes |
| **Intermediate Likelihood** |
| Absence of high-likelihood features and any of the following: |
| Typical angina in a patient without prior documented angina |
| Atypical anginal symptoms in diabetics or in nondiabetics with two or more other risk factors |
| Male gender |
| Age >70 |
| Extracardiac vascular disease |
| T-wave inversion of at least 1 mm in leads with dominant R waves |
| **Low Likelihood** |
| Absence of high- or intermediate-likelihood features but may have: |
| Chest pain, probably not angina |
| One risk factor but not diabetes |
| T waves flat or inverted <1 mm in leads with dominant R waves |
| Normal ECG |

## ELECTROCARDIOGRAM

In unstable angina, ST-segment depression, temporary elevation of ST segment, and inversion of T wave is seen in up to thirty to fifty percent of patients. In patients with the symptoms and signs of unstable angina, occurrence of new ST segment changes, as small as 0.05 mill volt, is an important finding and it is associated with poor prognosis. ECG changes in T-wave are sensitive for myocardial ischemia but are specific, only when they are new, deeper and magnitude of T wave inversions is 0.3millivolt.

## CARDIAC BIOMARKERS

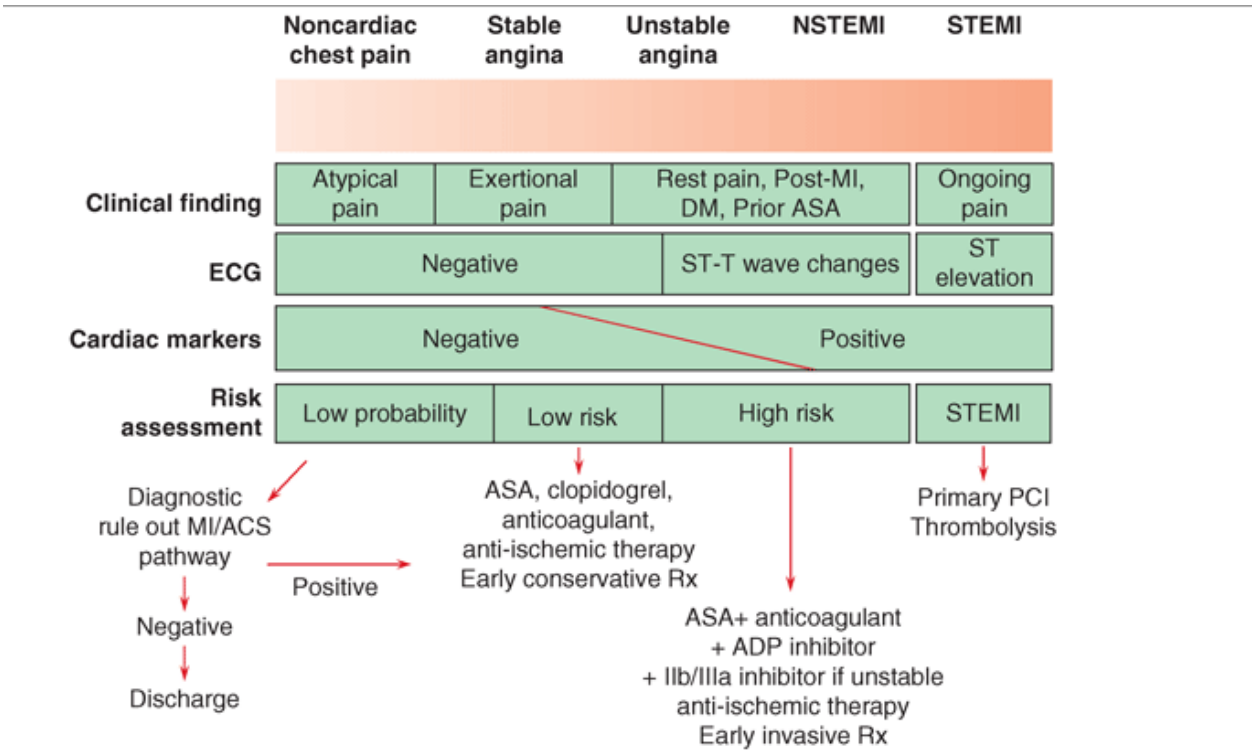
Patients who has unstable angina/NSTEMI and have elevated cardiac enzymes indicating death of the myocardium, such as Troponin and CPK-MB [this is a specific and sensitive indicator of myocardial cell necrosis], and are at increased risk for death or recurrent MI. When levels of these cardiac bio markers increase it helps to differentiate patients with NSTEMI and UA.

There is a positive correlation between the level of troponin increase and death rate. However minor elevations in troponins have been seen in patients without myocardial ischemia and is be due to congestive cardiac failure, myocarditis, or systemic embolism, or it may be false positive feature. Thus, in patients without clear history, mild elevations in troponin cannot be used for diagnosis of myocardial ischemia.

## ST ELEVATION MYOCARDIAL INFARCTION

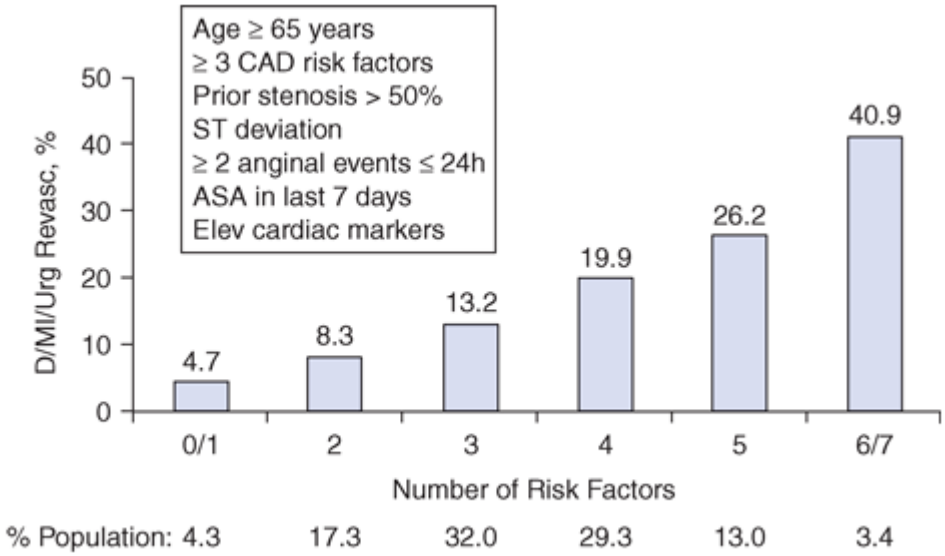
Chest Pain is the most common presenting feature seen in patients with ST elevation MI. The location of pain is deep and visceral patient commonly describes it as squeezing and crushing but uncommonly it is described as stabbing or burning in nature. It is similar in character to the pain occurring in angina pectoris but the differentiating feature is it occurs at rest, is usually more severe, and duration is longer.

**FIG: 1.5 ALGORITHMS FOR RISK STRATIFICATION AND MANAGEMENT OF PATIENTS WITH SUSPECTED ISCHEMIC HEART DISEASE**




Typically the pain is localized to the centre of the chest and/or the epigastrium, and, on occasion, it may present as radiating pain to the arms. Less commonly it also radiates to abdomen, neck, back, lower jaw and the most common location of the pain is beneath the xiphoid and epigastrium. The pain of STEMI may radiate as high as the occipital area but never present as pain below the level of umbilicus. It is commonly associated with diaphoresis, nausea, vomiting, anxiety, and a sense of impending doom.

**FIG: 1.6 TIMIRISK SCORE FOR UNSTABLE ANGINA/ NSTEMI**




**ON EXAMINATION**

Patients with MI appear anxious and are uncomfortable. Those with marked left ventricular (LV) failure at the time of presentation may have

1. Tachycardia,

2. Pulmonary creps,

3. Tachypnea,

4. Third heart sound.

Mitral regurgitant murmur when presents it suggests dysfunction of the mitral valve apparatus due to ischemia, rupture of chordae tendinae, or ventricular remodelling [27].

Patients with infarction of the right ventricle, have raised jugular venous pressure, Kussmaul sign (increase in JVP with inspiration),and a third heart sound due to right ventricular dysfunction may be present. Such patients usually have associated inferior infarctions, usually without evidence of left-heart failure.

**ELECTROCARDIOGRAM**

In a patient having active chest pain, the following features when present STEMI can be diagnosed [28-29].

A]. ST-segment elevation ≥ 1 mm (0.1 mV) in two or more adjacent limb leads (from aVLto III, including -aVR),

B]. ST-segment elevation ≥ 1 mm (0.1 mV) in chest leads V4 through V6,

C]. ST-segment elevation ≥ 2 mm (0.2 mV) in chest leads V1 through V3, ].

D].New left bundle-branch block.

Myocardial infarction evolves through three phase and its characteristics ECG findings are as follows.

1. The hyperacute phase

A]. Increased R wave amplitude.

B]. Increased ventricular activation time

C].Tall and widened T wave

D]. Slope ST Segment elevation.

2. The fully evolved phase;

A]. QS or QR complex, loss of R wave amplitude

B]. Coved ST segment elevation.

C] .Symmetrical pointed T wave inversion.

3. The chronic stabilised phase

A]. Prominent Q waves.

B]. Isoelectric ST segment.

C].Upright T wave.

## BIOMARKERS USED IN MI

Relative index which is the ratio of CKMB mass: CK activity -2.5 suggests of a myocardial source for the CKMB elevation.

## FIG: 1.7 CARDIAC BIOMARKERS CHARACTERSTICS FEATURES

| Biomarker | Molecular Weight (D) | Range of Times to Initial Elevation (hr) | Mean Time to Peak Elevations (Nonreperfused) | Time to Return to Normal Range |
|---|---|---|---|---|
| **Frequently Used in Clinical Practice** | | | | |
| MB-CK | 86,000 | 3–12 | 24 hr | 48-72 hr |
| cTnI | 23,500 | 3–12 | 24 hr | 5-10 d |
| cTnT | 33,000 | 3–12 | 12 hr-2 d | 5-14 d |

## ECHOCARDIOGRAM

Areas of abnormal regional wall motion are observed virtually in all patients with MI, and the degree of wall motion abnormality can be categorized with a semi quantitative wall motion score index, abnormal wall motion is less often noted echocardiographically when the infarction involve small area and the age of regional wall motion abnormality cannot be determined. Left ventricular function can be estimated from 2D echo and is useful in establishing prognosis after myocardial infarction.

The early use of echocardiography can be used in the early detection of potentially viable but stunned myocardium (contractile reserve), patients at risk for the development of congestive heart failure following MI, and mechanical complications.

## DIAGNOSIS

STEMI is diagnosed if patient has any two of the following.

A].Patient with ischemic discomfort

B]. ST elevation in electrocardiogram

C]. Rise in serum biomarker.

**TABLE:4 KILLIP'SCLASSIFICATION OF PATIENTS WITH ACUTE MI**.

| Killip class | Hospital mortality (%) |
|---|---|
| I No congestive heart failure | 6 |
| II Mild congestive heart failure, rales, $S_3$, congestion on chest radiograph | 17 |
| III Pulmonary edema | 38 |
| IV Cardiogenic shock | 81[a] |

## TABLE:5 LOCALISATION OF MI AND ITS SPECIFIC COMPLICATION

| ST Elevations | Affected Coronary Artery | Area of Damage | Complications |
|---|---|---|---|
| $V_1$ through $V_4$ | Left coronary artery: Left anterior descending | Anterolateral heart wall<br>Septum<br>Left ventricle<br>His bundle<br>Bundle branches | Left ventricular dysfunction: Decreased carbon dioxide, congestive heart failure<br>Left bundle-branch block<br>Right bundle-branch block<br>Left posterior fascicular block<br>Infranodal block (2° or 3°) |
| $V_5$ through $V_6$, I, aVL | Left coronary artery: Left circumflex branch | Left lateral heart wall | Left ventricular dysfunction: Decreased carbon dioxide, congestive heart failure<br>Infranodal block (2° or 3°) |
| II, III, aVF, $V_4R$ | Right coronary artery: Posterior descending branch | Inferior heart wall<br>Right ventricle | Hypotension (particularly with nitroglycerin and morphine, which can decrease preload)<br>Supranodal 1° heart block<br>Atrial fibrillation/flutter, premature atrial contractions<br>Infranodal block (2° and 3°)<br>Papillary muscle rupture (murmur) |
| $V_8$ and $V_9$ (or ST depressions in $V_1$ and $V_2$) | 90% Right coronary artery: Posterior descending branch<br><br>10% Left coronary artery: Left circumflex branch (will see elevations in $V_5$ through $V_6$) | Posterior heart wall | Hypotension<br>Supranodal 1° heart block<br>Infranodal block (2° and 3°)<br>Atrial fibrillation/flutter, premature atrial contractions<br>Papillary muscle rupture (murmur) |

## DIFFERENTIAL DIAGNOSIS

For patients having acute chest pain, consider the following diagnoses:

• Aortic Dissection

• Pneumothorax

• Pulmonary embolism

• Myocarditis

• Pericarditis

• Oesophageal rupture or spasm

• Hypertensive urgency or emergency

• GERD

• Intercostal muscle strain

• Costochondritis

## TREATMENT

Nitrates are administered by sublingual route or it is given by oral spray (0.3–0.6 mg) in patient experiencing ischemic pain. If patient have pain even after giving 3 doses, intravenous NTG [5–10 microgram/min] should be given. The rate of the infusion may be adjusted by increasing 10 microgram/min every three to five minutes till symptoms subsides or systolic blood pressure becomes less than 100 mmHg.

Hypotension and simultaneous intake of sildenafil group drugs in the previous one or two days are the important contraindication and nitrates are avoided in them.

## ANTITHROMBOTIC AGENTS

### Oral antiplatelet therapy

This forms the main component in the treatment of patients with unstable angina/NSTEMI. Initial treatment should include the administration of platelet COX inhibitor aspirin [30].The common starting dose is 325 mg/d, Low doses (75–160 mg/d) is given for long-term therapy. "Aspirin resistance" occurs in

five to ten percent of patients. Treatment with lower dose and non compliance to treatment are the reason suspected for this phenomenon.

The clopidogrel an inactive prodrug that is converted into an active metabolite, then it act by blocking the platelet ADP receptor, when used in combination with aspirin,it was shown to provide a twenty percent relative reduction death due cardiovascular events, MI, or stroke, compared with aspirin alone. This effect is seen in both low and high risk patients. Disadvantage of this combination is a moderate but absolute one percent increase in significant bleeding episode [31].

Pre-treatment with clopidogrel [300 or 600 mg loading dose, followed by 75 mg OD] is given prior to PCI.

The combination of clopidogrel and aspirin treatment for one year has been shown to benefit patient treated conservatively and PCI [32].

**HEPARIN**

The various options for anticoagulant therapy to be combined with aspirin and clopidogrel are as follows. Conventional heparin is the important mode of treatment. The low-molecular weight heparin, enoxaparin, is superior to UFH and it reduces further cardiac events, mainly in conservatively treated patients[33]. The fondaparinux, an indirect factor Xa inhibitoris same efficacy when compared with enoxaparin and it has the advantage of lower risk of major

bleeding. Bivalirudin, a direct thrombin inhibitor, also equal potency to either UFH or LMWH but when bivalirudin alone is used it has less bleeding when compared to the combination of heparin and a GP IIb/IIIa antagonist in patients with Unstable angina and non ST elevation MI undergoing catheterization and/or PCI [34].

**TABLE:6 CLINICAL USE OF ANTITHROMBOTIC AGENTS.**

| **Oral Antiplatelet Therapy** | |
|---|---|
| Aspirin | Initial dose of 162–325 mg nonenteric formulation followed by 75–162 mg/d of an enteric or a nonenteric formulation |
| Clopidogrel | Loading dose of 300-600 mg followed by 75 mg/d |
| Prasugrel | Pre-PCI: Loading dose 60 mg followed by 10 mg/d |
| **Intravenous Antiplatelet Therapy** | |
| Abciximab | 0.25 mg/kg bolus followed by infusion of 0.125 µg/kg per min (maximum 10 µg/min) for 12 to 24 h |
| Eptifibatide | 180 µg/kg bolus followed by infusion of 2.0 µg/kg per min for 72 to 96 h |
| Tirofiban | 0.4 µg/kg per min for 30 min followed by infusion of 0.1 µg/kg per min for 48 to 96 h |
| **Heparins*** | |
| Unfractionated Heparin (UFH) | Bolus 60–70 U/kg (maximum 5000 U) IV followed by infusion of 12–15 U/kg per h (initial maximum 1000 U/h) titrated to a PTT 50–70 s |
| Enoxaparin | 1 mg/kg SC every 12 h; the first dose may be preceded by a 30-mg IV bolus; renal adjustment to 1 mg/kg once daily if creatine Cl < 30 cc/min |
| Fondaparinux | 2.5 mg SC qd |
| Bivalirudin | Initial bolus intravenous bolus of 0.1 mg/kg and an infusion of 0.25 mg/kg per hour. Before PCI, an additional intravenous bolus of 0.5 mg/kg was administered, and the infusion was increased to 1.75 mg/kg per hour. |

## BETA BLOCKERS AND OTHER AGENTS

Beta blockers are the other main components of anti-ischemic treatment. Oral beta blocker titrated to achieve heart rate of 50–60 beats/min is the used as first-line treatment [35].

Intravenous beta blocker is used judiciously in patients with any evidence of acute heart failure, where it can increase the risk of cardiogenic shock. Drugs like diltiazem and others in calcium channel blockers group which act by decreasing heart rate are used in patients whose symptoms are not relieved despite treatment with maximum dose of nitrates and beta blockers and in patient whom beta blocker cannot be used due to contraindications. Other modes of therapy include ACE inhibitors and HMG-CoA reductase inhibitors – statins for long term secondary prevention of IHD [36]. Early intensive statin therapy (e.g., atorvastatin 80 mg) prior to percutaneous coronary intervention (PCI) has been shown to reduce complications hence high-dose statin therapy should be started at the time of admission.

## TABLE:7 SUMMARIES OF DRUGS USED IN ACS

| Drug Category | Clinical Condition | When to Avoid[a] | Dosage |
|---|---|---|---|
| Nitrates | Administer sublingually, and, if symptoms persist, intravenously | Hypotension<br>Patient receiving sildenafil or other PDE-5 inhibitor | Topical, oral, or buccal nitrates are acceptable alternatives for patients without ongoing or refractory symptoms<br>5–10 μg/min by continuous infusion titrated up to 75–100 μg/min until relief of symptoms or limiting side effects (headache or hypotension with a systolic blood pressure <90 mmHg or more than 30% below starting mean arterial pressure levels if significant hypertension is present) |
| Beta blockers[b] | Unstable angina | PR interval (ECG)<br>>0.24 s<br>2° or 3° atrioventricular block<br>Heart rate <60 beats/min<br>Systolic pressure <90 mmHg<br>Shock<br>Left ventricular failure<br>Severe reactive airway disease | Metoprolol 25–50 mg by mouth every 6 h<br>If needed, and no heart failure, 5-mg increments by slow (over 1–2 min)<br>IV administration |
| Calcium channel blockers | Patients whose symptoms are not relieved by adequate doses of nitrates and beta blockers, or in patients unable to tolerate adequate doses of one or both of these agents, or in patients with variant angina | Pulmonary edema<br>Evidence of left ventricular dysfunction (for diltiazem or verapamil) | Dependent on specific agent |
| Morphine sulfate | Patients whose symptoms are not relieved after three serial sublingual nitroglycerin tablets or whose symptoms recur with adequate anti-ischemic therapy | Hypotension<br>Respiratory depression<br>Confusion<br>Obtundation | 2–5 mg IV dose May be repeated every 5–30 min as needed to relieve symptoms and maintain patient comfort |

The above table shows various group of drugs used in ACS, their indication, dose and adverse effects.

## INVASIVE THERAPY

Early invasive therapy is given to patients with high risk,that is in patients having multiple clinical risk factors, ST-segment changes, and raised biomarkers. In this mode of therapy, following treatment with anti-ischemic and antithrombotic agents, coronary angiography is done within forty eight hours of admission [37-39], followed by coronary intervention procedure [PCI or coronary artery bypass grafting], depending on anatomy of coronary vessel.

## TABLE:8 INDICATIONS FOR EARLY INVASIVE THERAPY IN ACS.

| Class I (Level of Evidence: A) Indications |
|---|
| Recurrent angina at rest/low-level activity despite Rx |
| Elevated TnT or TnI |
| New ST-segment depression |
| Rec. angina/ischemia with CHF symptoms, rales, MR |
| Positive stress test |
| EF < 0.40 |
| Decreased BP |
| Sustained VT |
| PCI < 6 months, prior CABG |

## STEMI MANAGEMENT

The main goal of treating patient with STEMI should be rapid reperfusion to re-establish blood flow to ischemic myocardium. There are three main reperfusion strategies in practice currently [40]:

1] Thrombolytic therapy,

2] Primary PCI, and

3] Thrombolytic-facilitated primary PCI.

## THROMBOLYTIC THERAPY

It is an effective therapy in STEMI and should be given within 3 hrs of onset of chest pain for its maximal effect [41].

Class I

1. In the absence of contraindications, fibrinolytic drug can be given to

STEMI patients with symptom onset within the previous 12 hours and has ST elevation greater than 0.1 mV in at least two contiguous chest leads or at least two adjacent limb leads[42]. (Level of Evidence: A)

2. Fibrinolytic therapy is also indicated in STEMI patients with symptom onset within the prior 12 hours and new or presumably new onset LBBB. (Level of Evidence: A)

Class IIa

1. When there is no contraindication it is reasonable to administer fibrinolytic therapy to STEMI patients with symptom onset within the prior 12 hours and ECG finding shows true posterior MI. [Level of Evidence: C]

2. When there is no contraindications, it is justifiable to use fibrinolytic therapy to patients who has symptoms of STEMI beginning within the previous twelve to twenty four hours who have persistent ischemic symptoms and ST elevation greater than 0.1 millivolt in at least two continuous chest leads or in two adjacent limb leads. [Level of Evidence: B]

**Class III**

1. Fibrinolytic therapy is not used in asymptomatic patients whose symptoms of STEMI started more than 24 hours earlier. [Level of Evidence: C]

2. Fibrinolytic therapy is not used in patients whose ECG shows only ST-segment depression except if a posterior wall MI is suspected. [Level of Evidence;A]

**TABLE: 9.CONTRAINDICATION OF THROMBOLYTIC AGENTS**

| **Absolute Contraindications** |
|---|
| Any prior intracranial hemorrhage |
| Known structural cerebral vascular lesion |
| Known intracranial neoplasm |
| Ischemic stroke within the past 3 months (except for acute stroke within 3 hours) |
| Suspected aortic dissection |
| Active bleeding or bleeding diathesis (excluding menses) |
| Significant closed-head or facial trauma within 3 months |
| **Relative Contraindications** |
| History of chronic, severe, poorly controlled hypertension |
| Systolic pressure >180 mmHg or diastolic 110 mmHg |
| History of prior ischemic stroke >3 months previously, dementia, or known intracranial pathology not covered in absolute contraindications |
| Recent (within 2 to 4 weeks) internal bleeding |
| Noncompressible vascular punctures |
| Pregnancy |
| Active peptic ulcer |
| Current use of anticoagulants: the higher the international normalized ratio, the higher the risk of bleeding |
| For streptokinase/anistreplase: prior exposure (more than 5 days previously) or prior allergic reaction to these agents |

## TABLE: 10 FIBRIN SPECIFIC THROMBOLYTIC AGENTS

| Characteristic | Alteplase (tPA) | Reteplase (rPA) | Tenecteplase (tPA) | Lanoteplase (nPA) |
|---|---|---|---|---|
| Immunogenicity | No | No | No | ? |
| Plasminogen activation | Direct | Direct | Direct | Direct |
| Fibrin specificity | ++ | + | +++ | + |
| Plasma half-life | 4 to 6 min | 18 min | 20 min | 37 min |
| Dose | 15-mg bolus plus 90-min infusion up to 85 mg | 10+10-MU double bolus 30 min apart | ± 0.5 mg/kg single bolus | 120 KU/kg single bolus |

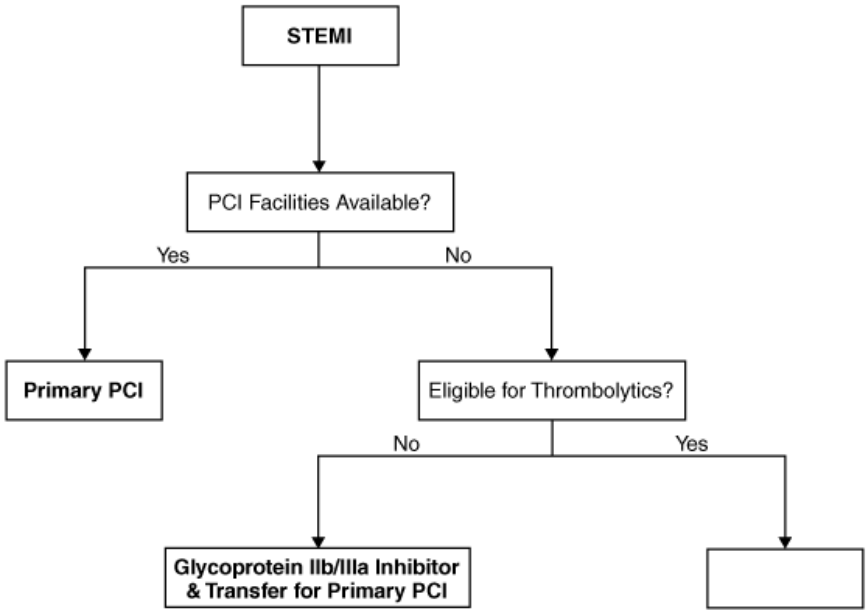
## PRIMARY PCI

95 percent of patients treated with primary PCI obtain complete perfusion where-as only 50 to 60 percent of patients has complete reperfusion when treated by thrombolysis [43]. Primary PCI has also advantage of lower risk of stroke and angiography quickly defines coronary anatomy, left ventricular (LV) function, and mechanical complications following MI.

## THROMBOLYTICS FACILITATED PCI

It refers to the pre-treatment with thrombolytic in STEMI patients before PCI and it act as a bridge therapy to immediate PCI. Currently it is not recommended as first line therapy [44-45].

**FIG: 1.8 ALGORITHMS FOR MANAGEMENT OF STEMI**




| Transport Time ("Incurred Ischemic Time") | Duration from Onset of Symptoms ("Fixed Ischemic Time") | |
|---|---|---|
| | 0–3 Hours | >3 Hours |
| 0–30 Minutes | PCI + GP IIb/IIIa | PCI + GP IIb/IIIa |
| 30–60 Minutes | Thrombolytic + Clopidogrel | PCI + GP IIb/IIIa |
| >60 Minutes | Thrombolytic + Clopidogrel | Thrombolytic + Clopidogrel or PCI + GP IIb/IIIa |

The above algorithm shows if facilities are available PCI is the preferred mode of intervention in STEMI patients. If not possible thrombolysis can be used.

## POTASSIUM AND ACUTE CORONARY SYNDROME

Acute coronary syndromes provide a useful clinical model for understanding of sympathetic stress as evidenced by number of classical symptoms such as excessive sweating and tachycardia. Hypokalaemia has been thought to be due to this mechanism.

Hypokalaemia can be considered as an acute phase response to sympathetic [46], Activation which occurs following myocardial ischemia and this subsequently activates sodium potassium- ATPase enzyme which is present on the cell membrane bound and shift potassium intracellularly.

ΔK = K at discharge - K on admission.

There are number of factors modifying the extent of the potassium dip (as indicated by ΔK) and serum glucose concentration during the period of ischemia was the only factor which was positively correlated with ΔK. On the other hand, HbA1c level was found to be inversely related with delta potassium [47].There was no relation between the intake of drug and ΔK [48].· The use of ACE-inhibitors, AR is not associated with change in delta potassium.

The other mechanism responsible for hypokalaemia in ACS is reactive increase in insulin [49] which occurs in response to adrenergic drive secondary to increases in serum glucose. This insulin in turn stimulates an intracellular shift of potassium into the cardiac and skeletal muscles by activating Na+/K+ATPase, which leads to the decrease in serum K level.

Raised blood glucose level during period of ischemia is strongly correlated with an high delta potassium[50]and it does not associate with of the severity of diabetes. These findings show that resistant to insulin may have a role in decreasing the potassium dip and that there is another serum potassium decreasing systems that may counteract the effects of insulin resistance [51].

The systemic sympathetic system is activated by stress of acute ischemia, and raised catecholamine's activates Na+/K+ATPase through β2 receptor. Previous use of non-selective beta blocker but not selective beta blocker use decrease ΔK.

Sodium-proton exchanger also activates the enzyme Na+/K+ATPase. Insulin can activate this exchanger. But diabetic condition – Hyperinsulinemia which is indicated by increased HbA1c,reduces ΔK. Hence other factors like intracellular acidification and some neurohumoral controllers, including the renin-angiotensin-aldosterone system may be involved in the activation of sodium proton exchanger when insulin resistance is present [52-55].

It is thought that the potassium which is a intracellular cation leak outside when cardiac cells are damaged by ischemic attacks and leads to an rise in serum potassium level during period of ischemia [thereby ΔK reduction] similar to cardiac markers like creatine kinase MB,but it is observed that a higher peak CK level occurs in patients with a greater ΔK and a lower potassium($K < 4.1$) at the time of admission however, the further analysis with Myocardial infarction demonstrated that ΔK was not significantly associated with peak CK

level , thus it is concluded that delta potassium reflects the severity of ischemic stress but not the extent of myocardial injury[56-58].

Patients with severe ischemia has lower K level on admission and patients with lower serum potassium level on admission was found to have a greater delta potassium[59-60] .But the patients who have with lower potassium level during ischemic attack did not have low potassium concentration during stable period. All these indicate that lower potassium patients are more prone to larger potassium dip and it indicates admission disease severity [61-65].

Low serum potassium concentration is seen in patients who presents earlier than those who came later. This Rapid recovery of serum potassium concentration has been found by serial blood sampling in patients with acute coronary syndrome [66].The early recovery in serum potassium value inpatients presenting later after the onset of chest pain is most likely because of sympathetic withdrawal and this causes intracellular potassium to returning to the systemic circulation. The evidence for an sympathetic mediated mechanism of increasing serum potassium value with later admission to hospital was provided by findings in patients pre-treated with beta blockers [67].In this group the early decrease in serum potassium values and later increase were not seen probably because adrenergic activation of sodium-potassium-ATPase was blocked, reducing potassium shift intracellularly. This effect was seen mostly in unstable angina patients and was less marked in acute infarction where the early decrease in potassium and its later recovery were preserved, albeit with loss of

significance[68-70]. This shows that sympathetic responses to coronary syndromes are associated to the extent of myocardial injury hence larger in acute myocardial infarction, and it has the potential to overcome any effects caused by pre medications.

Increased serum potassium value is seen in diabetic patients with acute coronary syndromes and this shows the importance of insulin in potassium homeostasis [71]. In Diabetes the early decrease in serum potassium concentration and its later recovery is not seen in unstable angina but occurs in acute myocardial infarction. In these regards, patients with diabetes mellitus behaves more likely patients treated with beta blockers, and autonomic dysfunction being the most possible aetiology for the effects on potassium[72]. Again it is reasonable to propose that the increased sympathetic response to acute infarction overcome the effect of diabetes in modifying serum potassium values.

Other evidence for sympathetic mechanisms causing early changes in serum potassium values in those patients without diabetes is provided by the inverse association between serum potassium within the first two hours of admission and various markers of sympathetic stress, including heart rate, hyper glycaemia, and bio markers of cardiac injury[73]. These associations were seen only in those patients without diabetes. Those who have the marked increase in heart rate, blood sugar, or creatine phosphokinase tended to have the larger reductions in serum potassium values that cannot modified by sympathetic

nerve dysfunction or beta blockade. Insulin resistance may be an important factor in the early decrease in serum potassium in diabetes patients by decreasing the intracellular potassium shift early after the onset of symptoms. The findings of stable blood glucose values in n patients without diabetes during the early periods after the onset of chest pain, during which potassium concentrations varies rapidly, suggest that sympathetic mechanisms were more important than insulin in shifting potassium across the cell membrane [74-77]. Sympathetic nerve dysfunction is a common finding in autonomic neuropathy, which can occur in forty percent of selected diabetic patients.A much greater percentage of patients may have minimal change of sympathetic functions as shown by myocardial radio labelled hydroxyephedrine uptake study using positron emission tomography. The association of autonomic nerve dysfunction in diabetes with a poor outcome and sudden cardiac death is well known fact. Prolongation of the QT interval, exaggeration of exertional ischemia, and dysregulation of sympathetically mediated cardiac blood flow are possible mechanisms. In diabetes increased serum potassium value in early period after the onset of symptoms in acute coronary syndromes is not thought to be harmful and may be beneficial in protecting against lethal ventricular arrhythmias [78]. Thus, while diabetes may be related with severe coronary syndromes, there are no evidence to shows it is associated with lethal ventricular arrhythmias [79].

**TABLE 11: IMPACT OF DELTA POTASSIUM AND DISEASE SEVERITY**

| | ΔK < 0.3 (n = 136) | ΔK≧0.3 (n = 175) | |
|---|---|---|---|
| Time of hospital stay (days) | 10.5 ± 10.8 | 13.8 ± 8.9 | P = 0.0039 |
| Myocardial Infarction | 59 (43.4%) | 124 (70.9%) | P < 0.001 |
| Peak Creatine Kinase (U/L) | 1010.0 ± 1540.3 | 2004.1 ± 2329.0 | P < 0.001 |

**TABLE 12: IMPACT OF POTASSIUM LEVEL AT ADMISSION AND DISEASE SEVERITY**

| | K≧4.1 (n = 169) | K < 4.1 (n = 142) | |
|---|---|---|---|
| Time of hospital stay (days) | 11.6 ± 9.5 | 13.2 ± 10.3 | NS |
| Myocardial Infarction | 88 (52.1%) | 95 (66.9%) | P = 0.011 |
| Peak Creatine Kinase (U/L) | 1343.5 ± 1853.7 | 1838.3 ± 2296.3 | P = 0.04 |

The above tables show that when potassium is low at the time of admission, patients have long duration of stay and increased myocardial infarction.

## METHODS AND MATERIALS:

## STUDY GROUP:

**Patients with acute coronary syndrome**

**1] STEMI**

**2] UNSTABLE ANGINA**

**3] NSTEMI**

**STUDY DESIGN:** CROSS SECTIONAL STUDY.

**MATERIALS:** Detailed history, Physical examination, ECG, 2D Echocardiography, Chest x-ray, Complete Haemogram,RBS, Blood urea, Serum Creatinine, Serum potassium, cardiac enzyme CPK-MB,Urine Routine, Total Cholesterol, Triglyceride levels.

**PLACE OF STUDY:** Govt. Kilpauk medical college hospital

**COLLABORATING DEPARTMENT:** Department of Cardiology, KMCH and Department Of Biochemistry

**DURATION OF STUDY:** 6 months

**CONSENT:**After obtaining written informed consent

**CONFLICT OF INTEREST**: Nil

**METHODOLOGY:1)**Potassium dip will be assessed by Δk-potassium at the time of discharge – potassium at the time of admission.

2) Severity of ACS assessed by

a) Duration of hospital stay

b) 2D echo

c) Cardiac enzyme cpk-mb assay.

**INCLUSION CRITERIA:**

1. All patients > 35 yrs of age admitted with 1$^{st}$ episode of acute coronary syndrome,

**EXCLUSION CRITERIA:**

1. Previous history of CAD.
2. Patients with CKD.
3. Patients on potassium controlling agents like ACE inhibitors, diuretics etc.

## DATA COLLECTION:

The data of each patient is collected in a specifically prepared proforma and includes Demographic details, Proper history, Past medical history, Clinical Features, ECG, Echocardiography, Chest x-Ray, Rbs,serum potassium, CPK-MB Level, Blood Urea, Serum Creatinine, Total Cholesterol and Triglyceride levels.

## STATISTICAL ANALYSIS

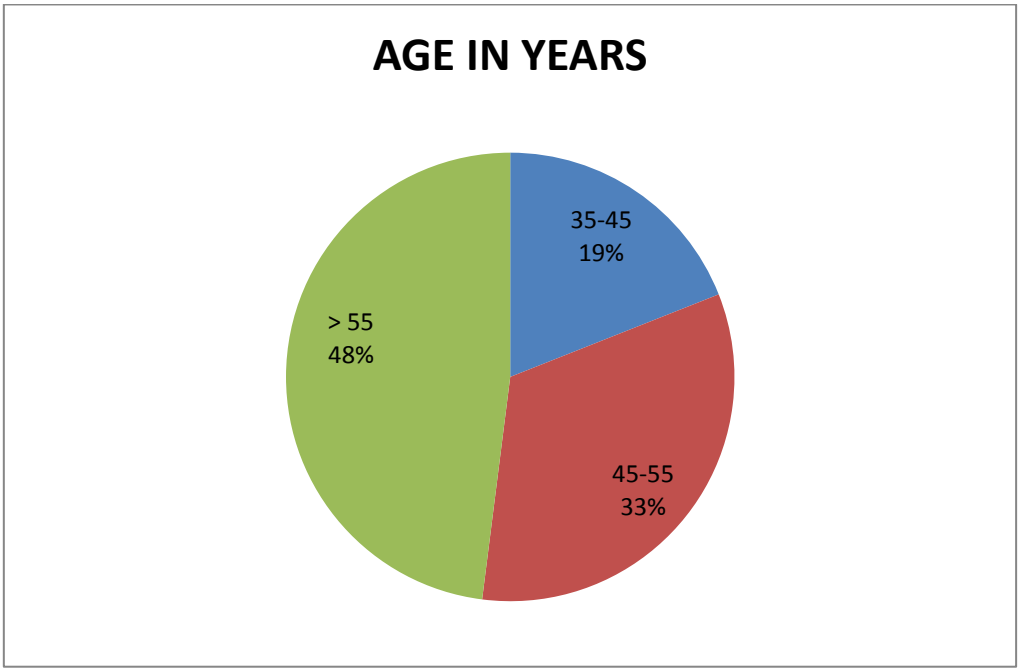
Statistical analysis was done to identify significance and correlation betweenpotassium dip and severity of acute ischemic stress in patients with acute coronary syndrome. Statistical analysis was done using Statistics Products Services Solutions (SPSS 15) software. Univariate analysis was done with paired t test and Pearson product moment correlation coefficient. A chi squared test was used to analyze the probability of differences in frequency distributions between the groups and $p<0.05$ was taken to be statistically significant in all calculations.

## RESULTS AND ANALYSIS

### TABLE:13. AGE WISE CASE DISTRIBUTION

| Age in years | | Frequency | Percent |
|---|---|---|---|
| | 35-45 | 19 | 19.0 |
| | 45-55 | 33 | 33.0 |
| | > 55 | 48 | 48.0 |
| | Total | 100 | 100.0 |

### FIG 2.1 DISTRIBUTION OF CASES IN AGE GROUP



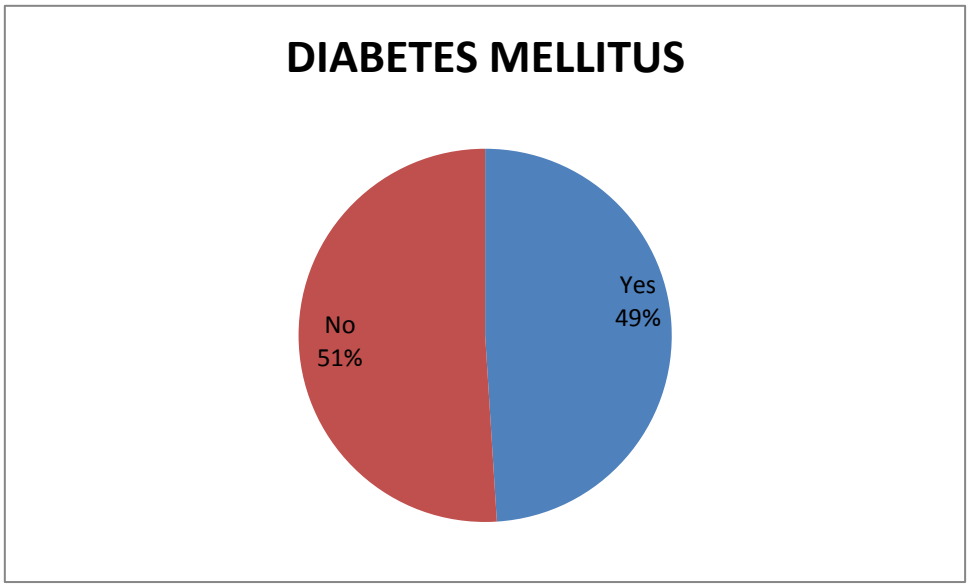

The study group selected consist of three groups. Patient in age between 35 to 45years, another in 46to 55 and final group more than 55. Most of the patient

are in final group. 48% were more than 55 years of age.

**TABLE 14 -DM IN STUDY GROUP**

| DIABETES | | Frequency | Percent |
|---|---|---|---|
| Valid | Yes | 49 | 49.0 |
| | No | 51 | 51.0 |
| | Total | 100 | 100.0 |

**FIG: 2.2 SHOWINGDM IN STUDY GROUP**

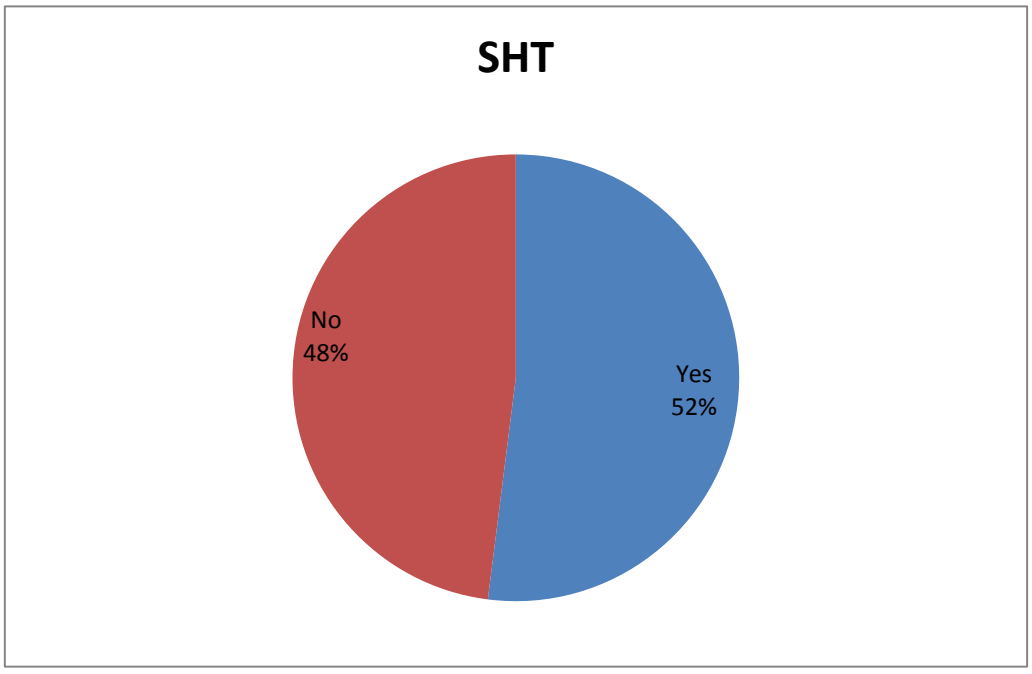



49% of the patients with acute coronary syndrome in this study group had diabetes mellitus.

## TABLE: 15 SHT IN STUDY GROUP

| SHT | | Frequency | Percent |
|---|---|---|---|
| Valid | Yes | 52 | 52.0 |
| | No | 48 | 48.0 |
| | Total | 100 | 100.0 |

## FIG 2:3 SHT IN STUDY GROUP

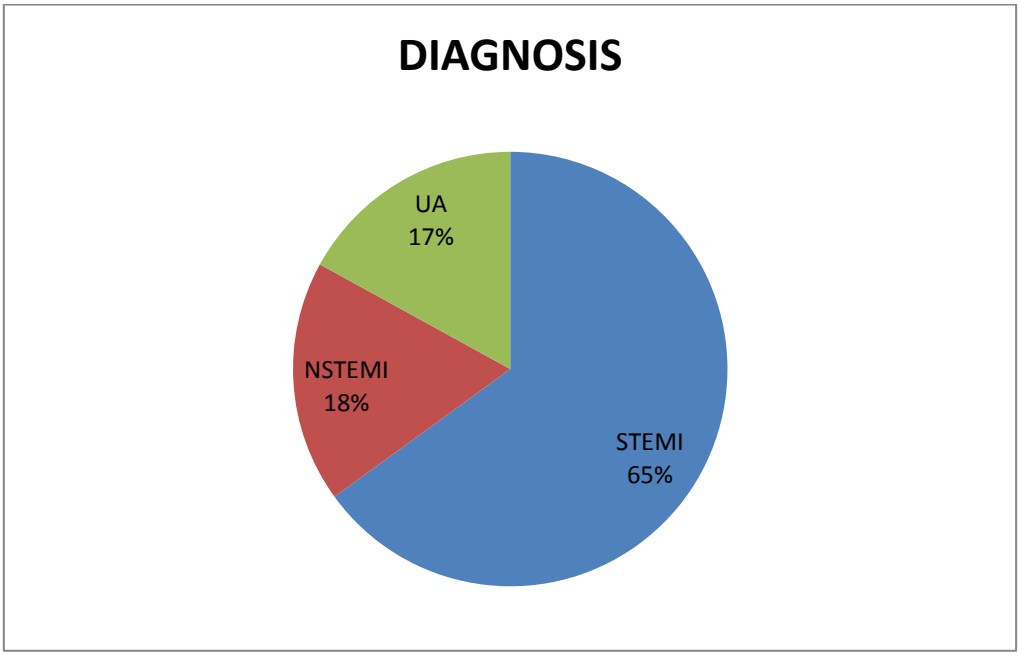



52% of the patients with acute coronary syndrome in this study group have systemic hypertension.

## TABLE 16: DIAGNOSIS IN STUDY GROUP

| GROUP | Frequency | Percent |
|---|---|---|
| STEMI | 65 | 65.0 |
| NSETMI | 18 | 18.0 |
| UA | 17 | 17.0 |
| Total | 100 | 100.0 |

## FIG: 2.4.DIAGNOSIS IN ACS




Patients with acute coronary syndromes were categorised in to three groups. Those with angina features, who have ST elevation in ECG, are diagnosed to have STEMI [ST elevation myocardial infarction]. Those with angina ECG

changes [no ST elevation] and raised cardiac biomarkers are diagnosed as NSTEMI. Those with angina, with ECG changes without raised biomarkers are diagnosed to have unstable angina.

Majority of the patient in the study groups has STEMI[65%], 18% HAS NSTEMI AND 17% has unstable angina.

**TABLE17. DURATION OF STAY**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | 5 days | 31 | 31.0 |
| | 6-7 | 46 | 46.0 |
| | > 7 | 23 | 23.0 |
| | Total | 100 | 100.0 |

Based on the duration of stay patients were divided into three groups. First group has duration of stay within 5 days and constitute 31% of the population in the study group. Those with duration of stay 6 and 7 days come under 2$^{nd}$ group and constitute 46%. Finally those who stayed for more than 7 days come under 3$^{rd}$ group and constitute 23%.

## FIG: 2.5. DURATION OF STAY OF PATIENTS

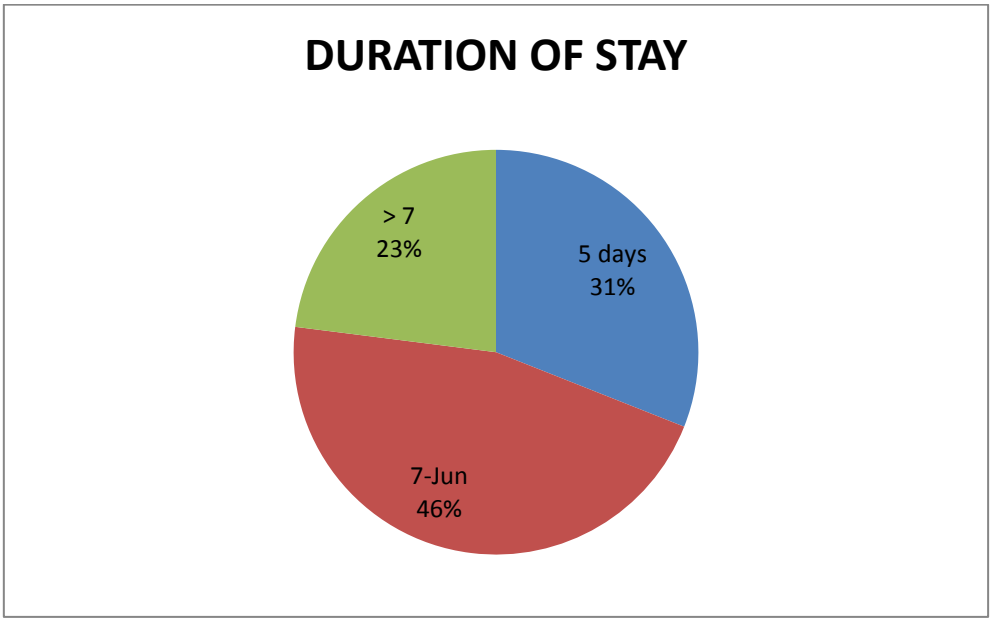



**TABLE.18.LEFT VENTRICULAR DYSFUNCTION**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | Normal | 17 | 17.0 |
| | Mild | 27 | 27.0 |
| | Moderate | 42 | 42.0 |
| | Severe | 14 | 14.0 |
| | Total | 100 | 100.0 |

Patients with normal left ventricular function based on 2D echocardiography constitute 17% in the study group. Patients with mild LV dysfunction [ejection fraction- 45 to 55%] constitute 27% of the study group. 42% of the study group

population has moderate LV dysfunction [EF- 30 to 45%]. Those with EF less than 30% have severe LV dysfunction and constitute 14% of the populations.

**FIG: 2.6 LV DYSFUNCTION IN STUDY GROUP**

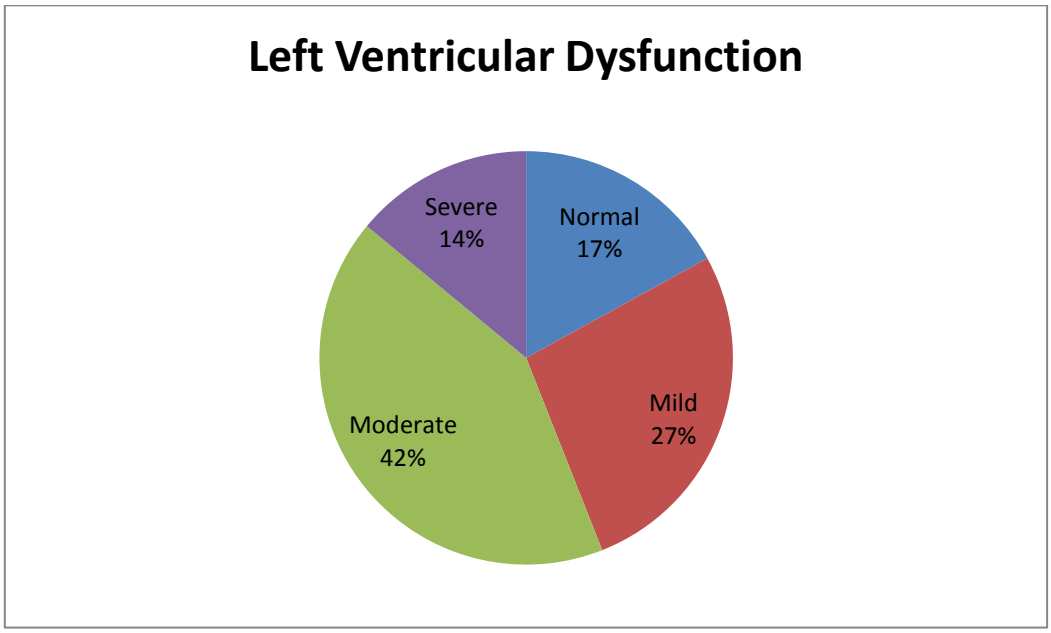
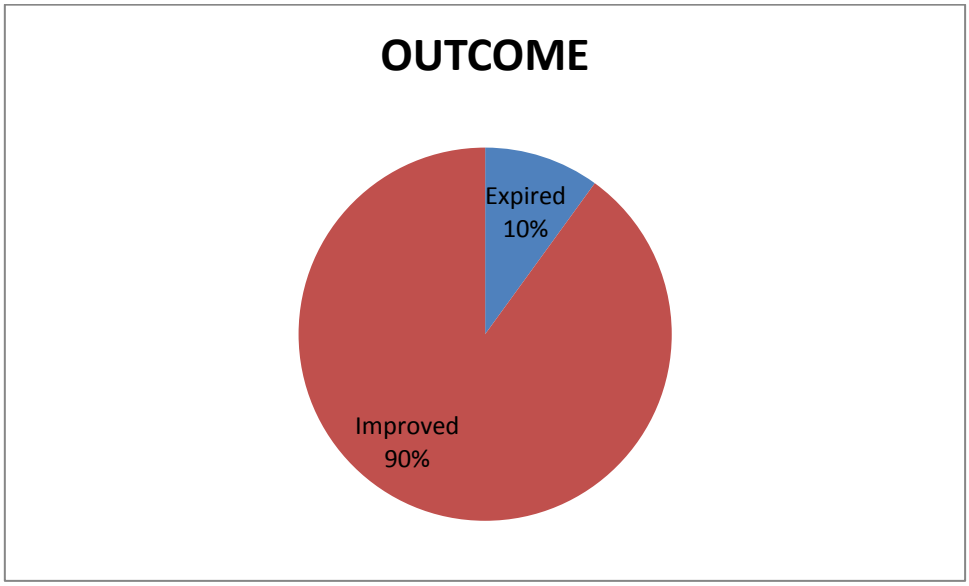



**TABLE.19. OUTCOME**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | Expired | 10 | 10.0 |
| | Improved | 90 | 90.0 |
| | Total | 100 | 100.0 |

## FIG: 2.7. OUTCOME IN STUDY GROUP

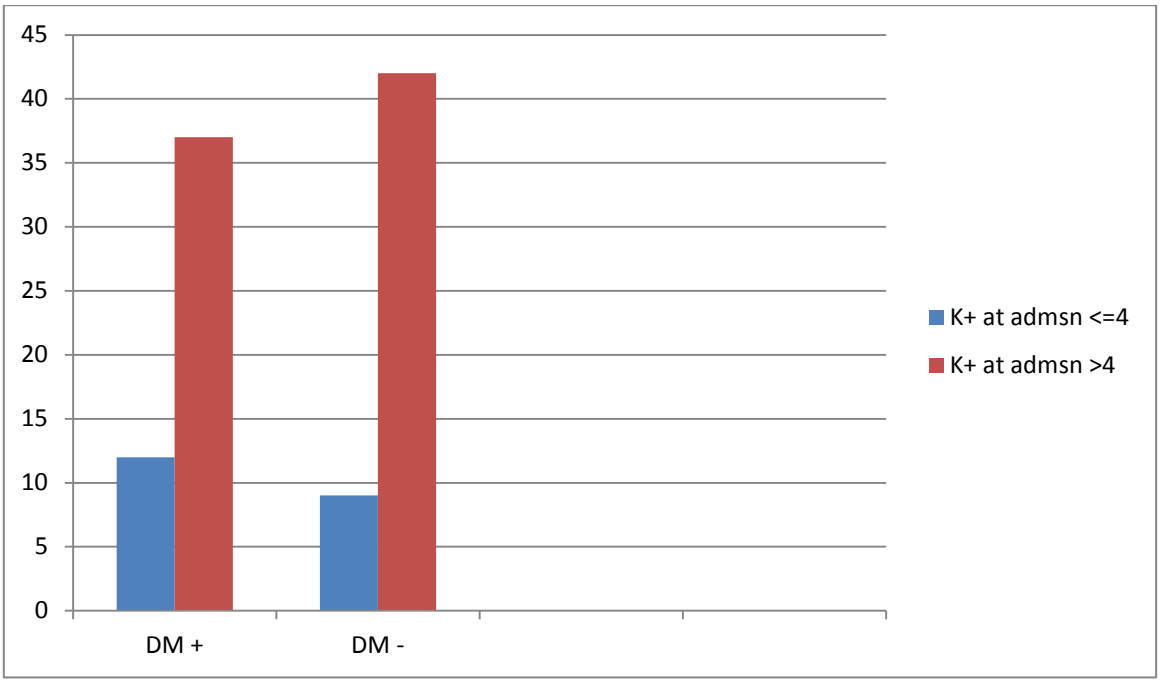



Of the study groups 90% improved and discharged from the hospital. 10% expired.

**TABLE .20.INFLUENCE OF DIABETICS ON THE POTASSIUM AT THE OF ADMISSION**

| | | | Potassium - Admission | | Total | P VALUE |
|---|---|---|---|---|---|---|
| | | | <= 4 | > 4 | | |
| DM | Yes | Count | 12 | 37 | 49 | 0.401 |
| | No | Count | 9 | 42 | 51 | |
| Total | | Count | 21 | 79 | 100 | |

## FIG:2.8 K AT ADMISSION AND DM




Of the 49% of the patients with diabetes mellitus only 12% has potassium less than 4 at admission and remaining 37% has potassium above 4 meq/l. On the other hand 21% of the patients with no DM have potassium less than 4 and remaining 42% has potassium greater than 4.

**TABLE 21.RELATION BETWEEN DURATION OF STAY AND POTASSIUM AT THE TIME OF ADMISSION**

| Duration of stay | | Potassium - Admission | | Total | P VALUE |
|---|---|---|---|---|---|
| | | <= 4 | > 4 | | |
| 5 days | Count | 6 | 25 | 31 | 0.964 |
| 6-7 | Count | 10 | 36 | 46 | |
| > 7 | Count | 5 | 18 | 23 | |
| Total | Count | 21 | 79 | 100 | |

Of the 31% of population with duration of stay within 5 days, only 6% has potassium less than 4 and remaining population has normal potassium. 10% of the population who stayed for 5 to 7 days has potassium less than 4. In Those who stayed for more than 7 days, only 5 patients have potassium less than 4.

## FIG: 2.9 K AT ADMISSION AND DURATION OF STAY

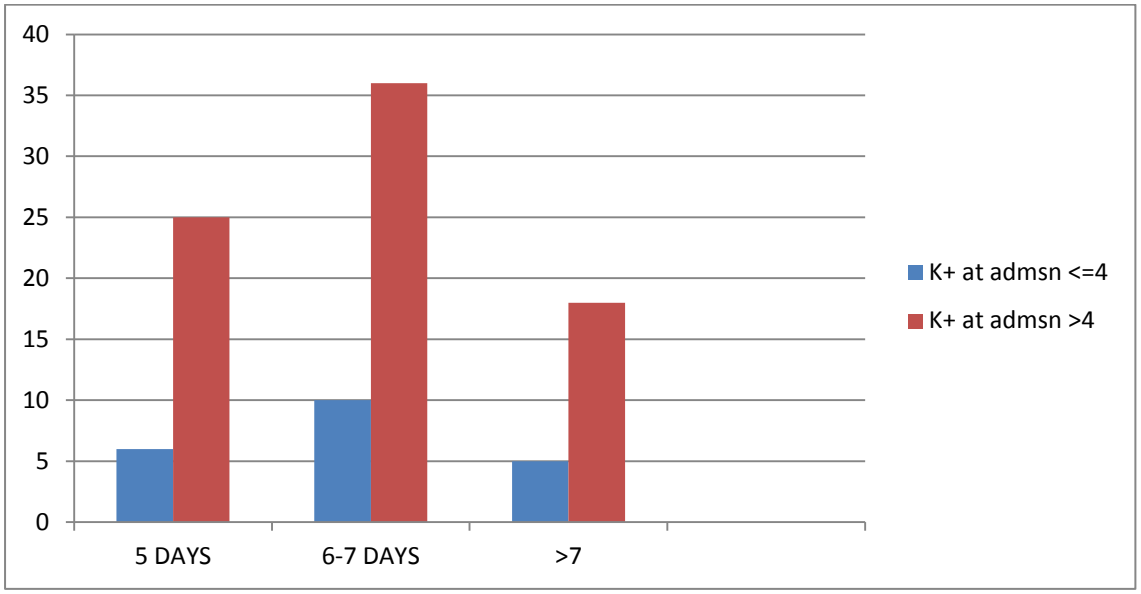



**TABLE 22.CORRELATION BETWEEN POTASSIUM AT ADMISSION AND THE LV DYSFUNCTION.**

| LV DYSFUNCTION | | Potassium - Admission | | Total |
|---|---|---|---|---|
| | | <= 4 | > 4 | |
| NORMAL | Count | 6 | 11 | 17 |
| | % within LVD | 35.3% | 64.7% | 100.0% |
| MILD | Count | 5 | 22 | 27 |
| | % within LVD | 18.5% | 81.5% | 100.0% |
| MODERATE | Count | 6 | 36 | 42 |
| | % within LVD | 14.3% | 85.7% | 100.0% |
| SEVERE | Count | 4 | 10 | 14 |
| | % within LVD | 28.6% | 71.4% | 100.0% |

35% of the patients with normal LV function have potassium dip. 19% of the patients with mild LV dysfunction have potassium less than 4. Of the 42

patients with moderate LV dysfunction only 14% has potassium dip. In patients with severe LV dysfunction only 28% has potassium less than 4 at the time of admission.

**FIG: 3.1 K AT ADMISSION AND LV DYSFUNCTION**

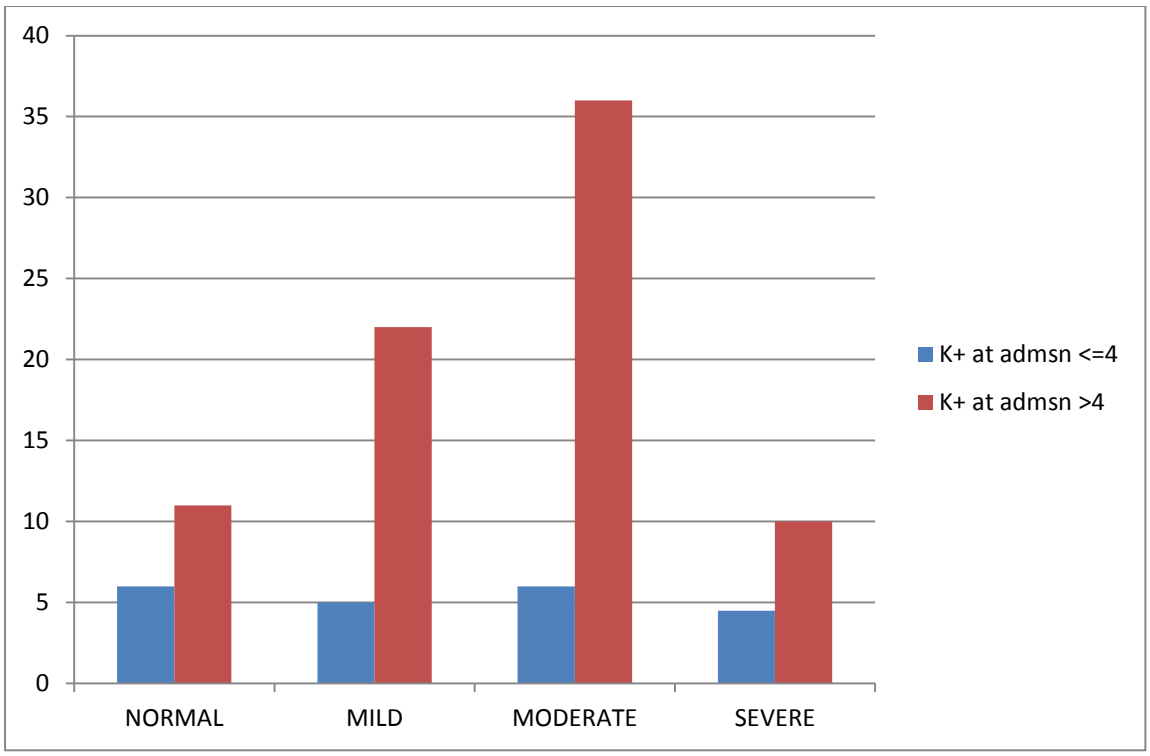
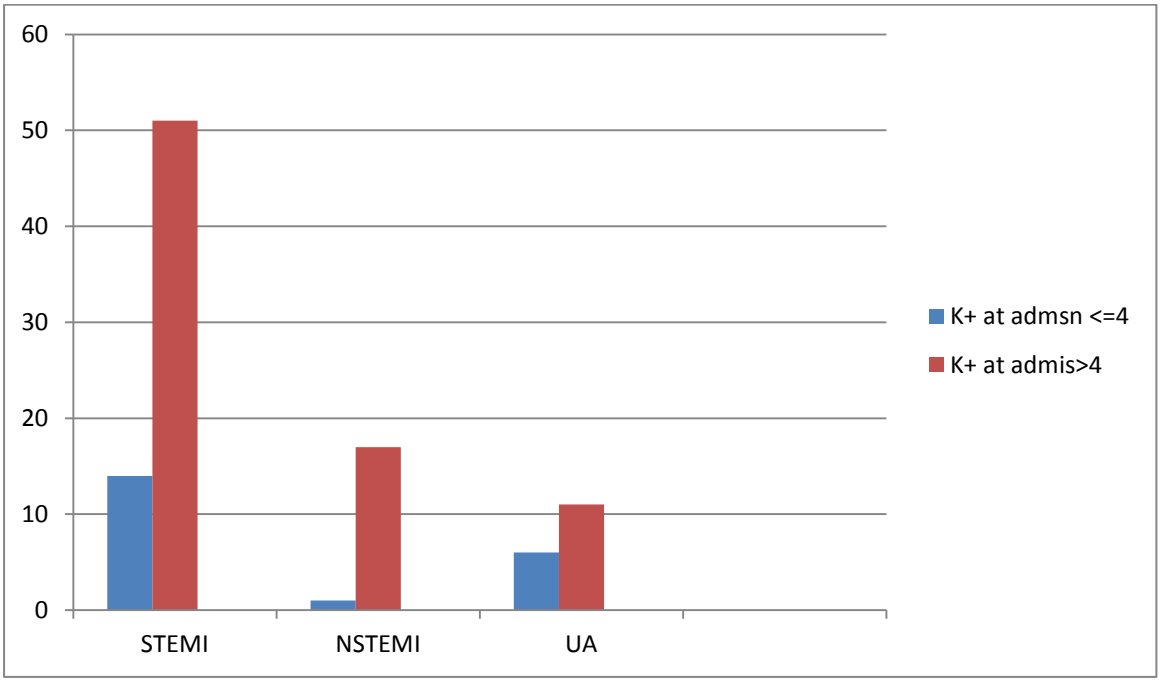


**TABLE 23.DISTRIBUTION OF POTASSIUM AT ADMISSION IN VARIOUS GROUP OF ACS**

| DIAGNOSIS | | Potassium - Admission | | Total | P VALUE |
|---|---|---|---|---|---|
| | | <= 4 | > 4 | | |
| STEMI | Count | 14 | 51 | 65 | 0.96 |
| | % within Diagnosis | 21.5% | 78.5% | 100.0% | |
| NSTEMI | Count | 1 | 17 | 18 | |
| | % within Diagnosis | 5.6% | 94.4% | 100.0% | |
| UA | Count | 6 | 11 | 17 | |
| | % within Diagnosis | 35.3% | 64.7% | 100.0% | |
| TOTAL | Count | 21 | 79 | 100 | |
| | % within Diagnosis | 21.0% | 79.0% | 100.0% | |

The relationship between potassium at the time of admission and various ACS group is shown in the above table. It is clear from the above table that it has no significant correlation.

## FIG: 3.2 K AT ADMISSION AND DIAGNOSIS

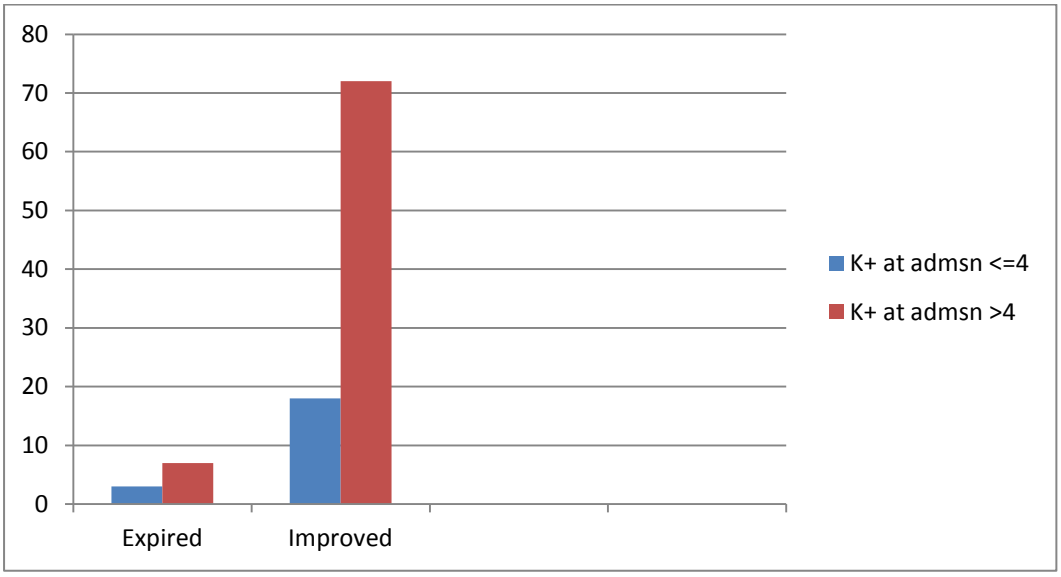



Among 65 of the STEMI patients 14% has potassium less than 4 and remaining has normal LV function. In 18 patients with NSTEMI ONLY 6% had potassium less than 4. 35% of the unstable angina patients have potassium less than 4. Overall 21% has potassium less than 4.

**TABLE 24.POTASSIUM VALUE AT ADMISSION AND OUTCOME**

| OUTCOME | | Potassium - Admission | | Total | P VALUE |
|---|---|---|---|---|---|
| | | <= 4 | > 4 | | |
| Expired | Count | 3 | 7 | 10 | 0.351 |
| Improved | Count | 18 | 72 | 90 | |
| Total | Count | 21 | 79 | 100 | |

**FIG: 3.3 K AT ADMISSION AND OUTCOME**




33% of the expired patients have potassium dip. Among 90% of the improved

patients 18% patients has potassium less than 4.

**TABLE.25. DELTA POTASSIUM AGE WISE DISTRIBUTION**

| Age | | Delta potassium [meq/l] | | Total | P VALUE |
|---|---|---|---|---|---|
| | | >0.5 | <0.5 | | |
| 35-45 | Count | 12 | 7 | 19 | 0.209 |
| 45-55 | Count | 17 | 16 | 33 | |
| >55 | Count | 34 | 14 | 48 | |
| TOTAL | Count | 63 | 37 | 100 | |

Delta potassium is defined as the difference in potassium at the time of discharge and admission value. 12 patients in the age 35 to 45 has delta potassium greater than 0.5. Among the 33 patients in the age group 45 to 55, 17 has delta potassium greater than 0.5. 70% of the patients in the age group more than 55 have significant delta potassium.

FIG: 3.4. DELTA K IN VARIOUS AGE GROUP

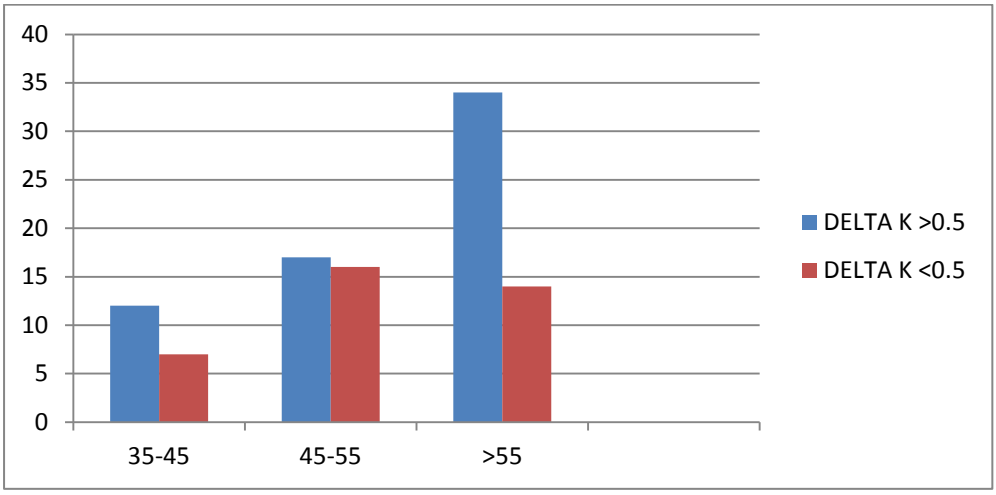
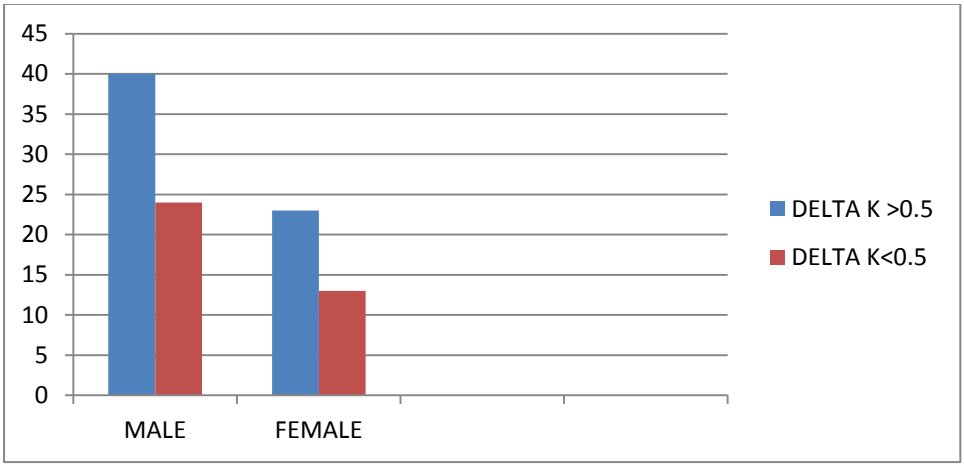



**FIG: 3.5. DELTA K AND SEX OF THE PATIENTS**




The above bar diagram shows the distribution of delta potassium and sex of the patients. Both have larger delta potassium.

**TABLE 26.DELTA POTASSIUM AND SEX OF THE PATIENTS**

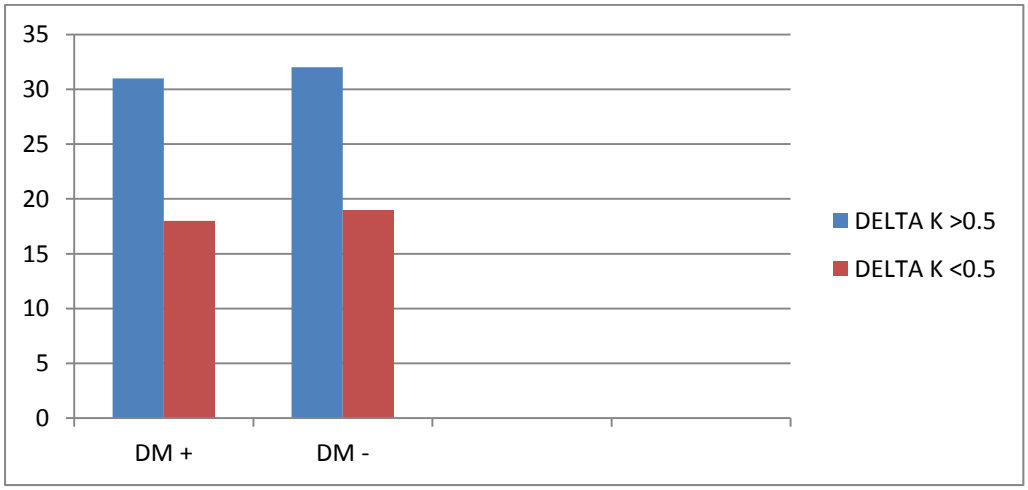
| Sex | | Delta potassium [meq/l] | | Total | P value |
|---|---|---|---|---|---|
| | | >0.5 | <0.5 | | |
| Male | Count | 40 | 24 | 64 | 0.89 |
| | % within Sex | 62.5% | 37.5% | 100.0% | |
| | % within Potassium - Difference | 63.5% | 64.9% | 64.0% | |
| Female | Count | 23 | 13 | 36 | |
| | % within Sex | 63.9% | 36.1% | 100.0% | |
| | % within Potassium - Difference | 36.5% | 35.1% | 36.0% | |
| Total | Count | 63 | 37 | 100 | |
| | % within Sex | 63.0% | 37.0% | 100.0% | |
| | % within Potassium - Difference | 100.0% | 100.0% | 100.0% | |

62% of the male has delta potassium greater than 0.5. Among 36 females 23 has delta potassium which is 63%. This shows there is no relation between sex and delta potassium.

**TABLE 2.DELTA POTASSIUM IN DIABETIC AND NON DIABETIC GROUP**

| Diabetes Mellitus | | Delta potassium [meq/l] | | Total | P VALUE |
|---|---|---|---|---|---|
| | | >0.5 | <0.5 | | |
| Yes | Count | 31 [63%] | 18 [37%] | 49 | 0.957 |
| No | Count | 32 [63%] | 19 [37%] | 51 | |
| Total | Count | 63 | 37 | 100 | |

## FIG: 3.6. DELTA K AND DM

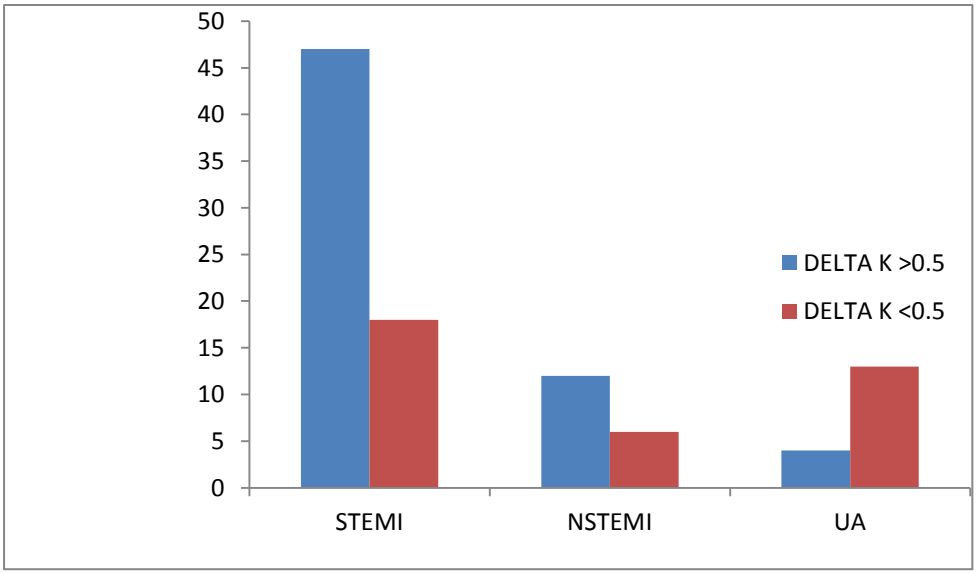



In both diabetics and non-diabetics 63% has delta potassium greater than 0.5 and others has delta potassium less than 37%.

**TABLE.28. DELTA POTASSIUM IN VARIOUS GROUPS**

| Diagnosis | | Delta potassium [meq/l] | | Total | p value |
|---|---|---|---|---|---|
| | | >0.5 | <0.5 | | |
| STEMI | Count | 47 | 18 | 65 | 0.001 |
| | % within Diagnosis | 72.3% | 27.7% | 100.0% | |
| NSTEMI | Count | 12 | 6 | 18 | |
| | % within Diagnosis | 66.7% | 33.3% | 100.0% | |
| UA | Count | 4 | 13 | 17 | |
| | % within Diagnosis | 23.5% | 76.5% | 100.0% | |
| TOTAL | Count | 63 | 37 | 100 | |
| | % within Diagnosis | 63.0% | 37.0% | 100.0% | |

**FIG: 3.7.DELTA POTASSIUM AND DIAGNOSIS**




From the above it is clear that delta potassium is greater in STEMI groups compared to others.

Among 65 of the STEMI patients 72% has delta potassium greater than0 .5 and remaining has low delta potassium. In 18 patients with NSTEMI 67% had potassium dip more than 0.5. 24% of the unstable angina patients have potassium dip of more than0.5 .Overall 63% has potassium dip.

**TABLE29. DELTA POTASSIUM AND DURATION OF STAY IN HOSPITAL**

| Duration of stay | | Delta potassium [meq/l] | | Total | P VALUE |
|---|---|---|---|---|---|
| | | >0.5 | <0.5 | | |
| 5 days | Count | 6 [19%] | 25 [81%] | 31 | 0.001 |
| 6-7 | Count | 35 [76%] | 11 [24%] | 46 | |
| > 7 | Count | 22 [95%] | 1 [5%] | 23 | |
| Total | Count | 63 | 37 | 100 | |

Of the 31 patients with duration of stay within 5 days, only 19% has delta potassium greater than 0.5 and remaining population has normal potassium. But 76%% of the population who stayed for 5 to 7 days has delta potassium greater than 0.5. In those who stayed for more than 7 days, 95% of patients has delta potassium more than 0.5%.

**FIG:3.8 DELTA POTASSIUM AND DURATION OF STAY**

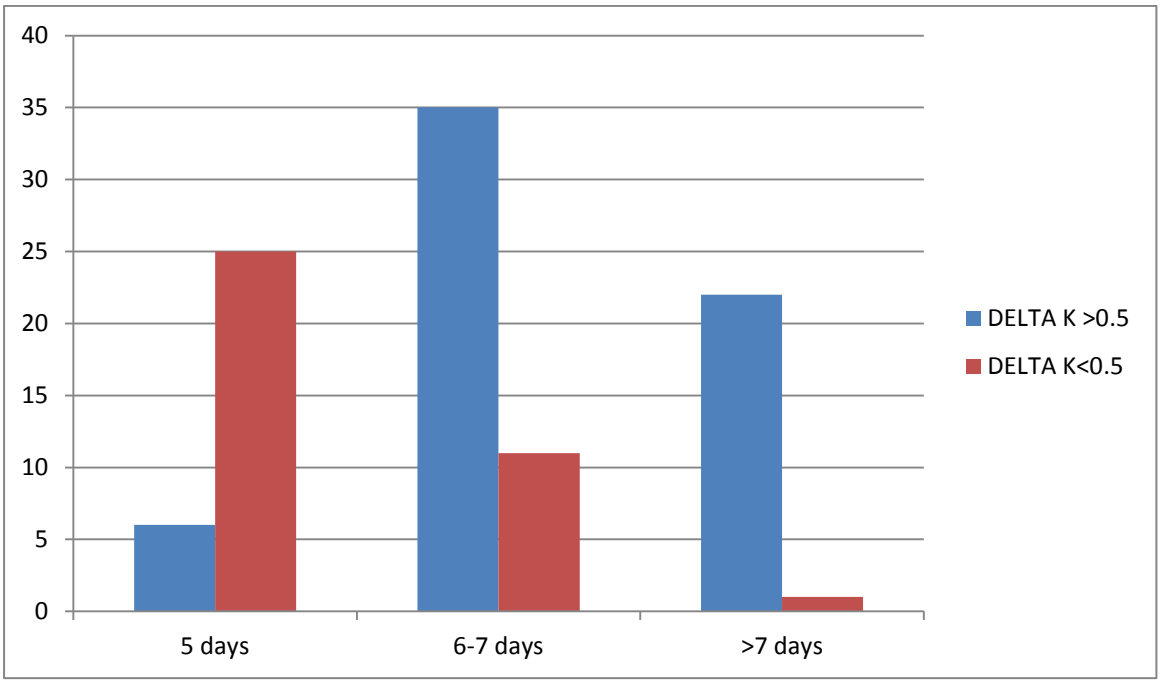


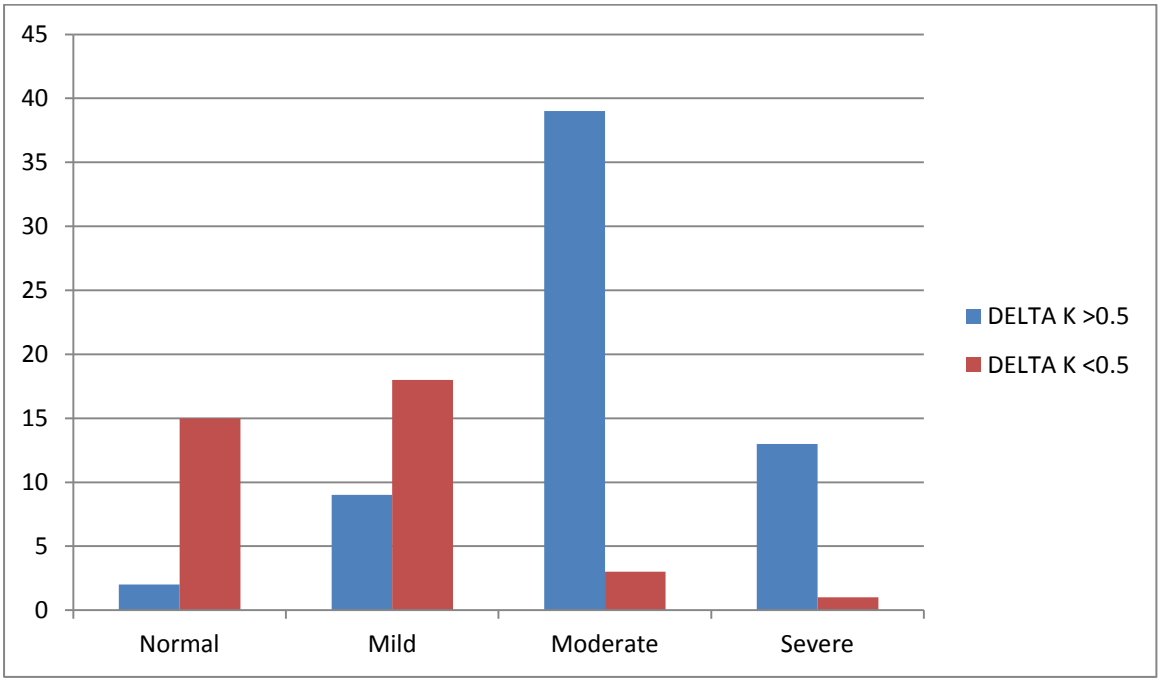
**TABLE30. DELTA POTASSIUM AND LV DYSFUNCTION**.

| LV Dysfunction | | | Delta potassium [meq/l] | | Total | p value |
|---|---|---|---|---|---|---|
| | | | >0.5 | <0.5 | | |
| A] | Normal | Count | 2 [12%] | 15 [88%] | 17 | 0.001 |
| B] | Mild | Count | 9 [50%] | 18 [50%] | 27 | |
| C] | Moderate | Count | 39 [93%] | 3 [7%] | 42 | |
| D] | Severe | Count | 13 [93%] | 1 [7%] | 14 | |
| Total | | Count | 63 | 37 | 100 | |

According to echocardiography findings of left ventricular function patients can be categorised into

Four groups A] Those with normal left ventricular function B] Mild left ventricular dysfunction C] Moderate left ventricular dysfunction D] Severe left ventricular dysfunction From the above table it is clear patient with greater left ventricular dysfunction has larger delta potassium.

## FIG: 3.9 DELTA K AND LV DYSFUNCTION



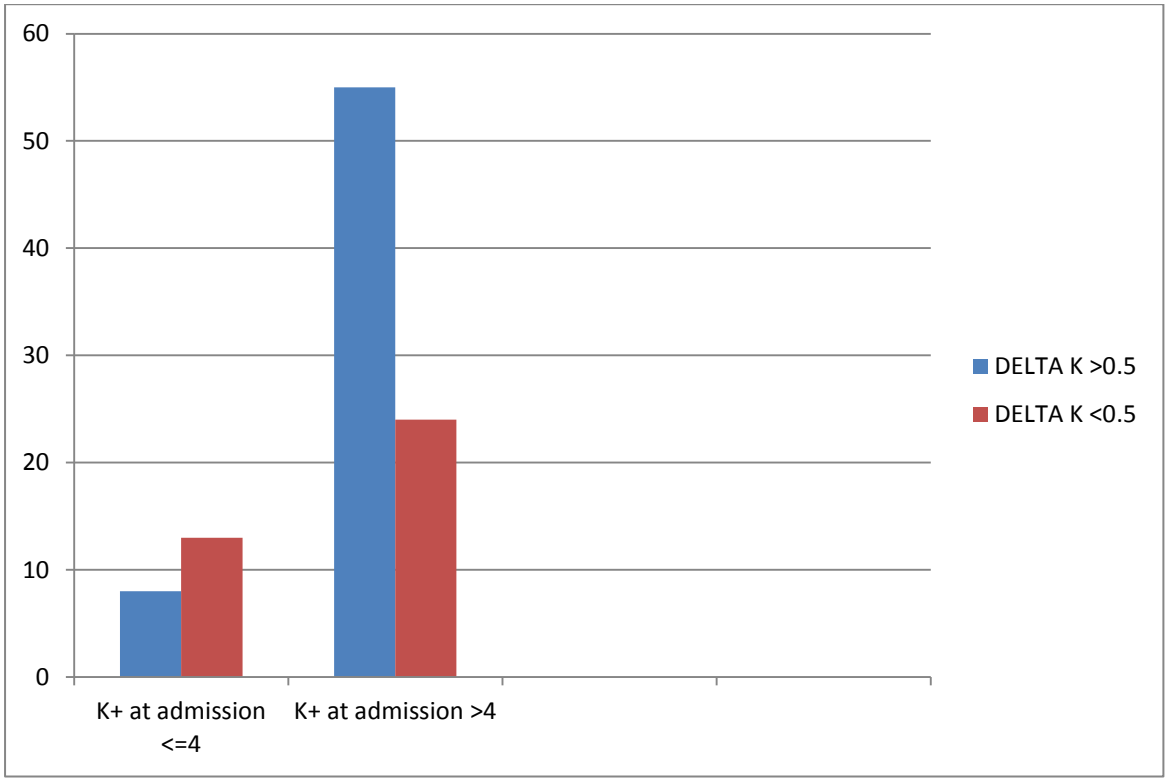

Only 12% of the patients with normal LV function has Delta potassium greater than 0.5.On the other hand 50% of the patients with mild LV dysfunction have delta potassium more than 0.5. Of the 42 patients with moderate LV dysfunction 93% has significant delta potassium. In patients with severe LV dysfunction93% has significant delta potassium.

**TABLE31. RELATIONSHIP BETWEEN DELTA POTASSIUM AND POTASSIUM AT ADMISSION**

| Potassium – Admission [mEq/L] | | Delta potassium [meq/l] | | Total | P value |
|---|---|---|---|---|---|
| | | >0.5 | <0.5 | | |
| <= 4 | Count | 8 [38%] | 13 [62%] | 21 | 0.08 |
| > 4 | Count | 55 [70%] | 24 [30%] | 79 | |
| Total | Count | 63 | 37 | 100 | |

38% of the patients with potassium less than 4 have significant delta potassium and 70% of the patients with no potassium dip have significant delta potassium.

## FIG: 4.1 DELTA K AND K+ AT ADMISSION




38% of the patients with potassium less than 4 has significant delta potassium and 70% of the patients with no potassium dip have significant delta potassium.

# DISCUSSION

Ischemic heart disease is the important cause of morbidity and mortality in India as well as in other countries. Acute coronary syndrome is the medical emergency. Because of high prevalence of risk factors like smoking, hypertension, diabetes mellitus, alcoholism together with adverse life style changes it's incidence is increasing day by day.

Patients presenting with acute coronary syndromes commonly have hypokalaemia, which increases the risk of serious ventricular arrhythmias. Hypokalaemia can be viewed as an acute phase response to sympathetic activation, which stimulates membrane bound sodium-potassium- ATPase and drives potassium intracellularly.

Prognosis in patients with acute coronary syndrome can be assessed by number of factors like associated failure signs, ejection fraction, raised biomarkers. Few studies have shown hypokalemia during episode of acute coronary syndrome can be associated with poor prognosis and adverse outcome.

The present study asses the correlation between delta potassium and severity ischemic stress. The severity is assessed by three factors.

1] Ejection fraction by 2D echo

2] Duration of hospital stay.

3] Rise in cardiac biomarkers.

Delta potassium is the difference between potassium at the time of discharge and at the time of admission. The study group consist of 100 patients admitted to cardiology with acute coronary syndrome.

One study has shown the decreased potassium value at the time of admission has associated with large delta potassium and adverse outcome. So we analysed the potassium value at the time of admission with severity of ischemic stress.

Majority of the patients admitted with ACS are more than 55 years of age, who constitute 48% of the study group. Among the study group 64% are male and 36% are female. 49% of the study group populations have diabetes mellitus.

in the study group 65% had STEMI, 18% has NSTEMI and 17% has UNSTABLE ANGINA.

## CORRELATION BETWEEN POTASSIUM VALUE AT THE OF ADMISSION AND SEVERITY OF ISCHEMIC STRESS

In patients with diabetes mellitus only 25% has low potassium below 4 meq/l. while others has value above 4. This reflects in diabetes mellitus the initial decrease in potassium value is not seen. This may be due to autonomic dysfunction associated with diabetes mellitus. This is is supported by the study by**27 Jarman**

**PR, Kehley AM, Mather HM. Hyperkalaemia in diabetes:prevalence and associations. Postgrad Med J 1995;71:551–2.**

1] Among three groups of ACS patients in STEMI patients only 21% has low potassium value. In NSTEMI patients only 5% has absolute potassium value less than 4 at the time of admission. In UNSTABLE ANGINA 35% has low potassium value. This shows that there is no correlation between potassium value at the time of admission and enzyme activity.

This may be due to difference in the time of admission which has impact on the potassium value at the time of admission. Only patients admitted earlier has low potassium value which gradually increases over time. This is supported by the study- **effect of diabetes on serum potassium concentrations inAcute coronary syndromes K Foo, N Sekhri, A Deaner, C Knight, A Suliman, K Ranjadayalan, A D Timmis.**

2]The relation between duration of hospital stay is also not positive as shown below.

GROUP A- those who stayed for less than 5 days- 19% has potassium less than 4. GROUP B- [those who stayed 5 to 7 days] 19% has low potassium value. GROUP C-[who stayed for more than 7 days] 21% has low potassium value.

3] The relation between LV dysfunction and low potassium value at the time of admission is also not positive. In patients with normal LV dysfunction 35% has low potassium value, while 18% of patients with mild LV dysfunction has low potassium value. In patient with moderate LV dysfunction 18% has low potassium. Finally in severe lv dysfunction group 28% has lowpotassium value. This may be also due to difference in the time of admission as explained above.

**RELATION BETWEEN DELTA POTASSIUM AND SEVERITY OF ISCHEMIC STRESS**

A] Among 65 patients with STEMI 47 had delta potassium value more than 0.5 which constitute 72%. In patients with NSTEMI 66% has significant delta potassium. But in UNSTABLE ANGINA group only 23% has delta potassium more than 0.5. This finding is consistent with the study**. herlitz j, hjalmarson a,bengtsona: occurrence of hypokalemia in suspected acute myocardial infarction and its relation to clinical historyand clinical course. clincardiol 1988, 11(10):678–682.**

B] Delta potassium has also shown to be positively correlated with duration of stay in hospital as shown below.

1] Patient who stayed for 5 or less- 19% has significant delta potassium

2] In the patient who stayed for 5 to 7- 76% has delta potassium more than 0.5

3] In patients who stayed for more than 7 days- 96% has significant delta k.

C] The relationship between delta potassium and LV dysfunction also correlate positively. In 17 patients with normal only 2 has delta potassium more than 2. In patients with mild LV dysfunction 33% has significant delta potassium. But 92% of patients with moderate and 93% of patients with severe LV dysfunction has delta potassium more than 0.5. This is also supported by the study **transient decrease in serum potassium levelduring ischemic attack of acute coronarysyndrome: hiroshi sekiyama1, tomohisa nagoshi1, kimiaki komukai1, masato matsushima2, daisuke katoh1, kazuo ogawa1,kosuke minai1, takayuki ogawa1 and michihiro yoshimura1.**

## CONCLUSION

1] Prevalence of potassium dip is common among patients with acute coronary syndrome.

2] Diabetic patients does not have significant delta potassium.

3] Low potassium value at the time of admission [less than 4] was not found to correlate with disease severity in this study.

4] Delta potassium was positively correlated with severity of ischemic stress in patients with ACS.

5] Age, sex, diabetes, SHT, dyslipidaemia, smoking and alcoholism do not have major impact on delta potassium.

## LIMITATION OF THE STUDY

1] Sample size was small and further studies with larger sample are necessary.

2] The study doesn't analyse the time of onset of pain and admission time which may have an impact in the potassium value at the time of admission.

3] The topic in general is new concept and few studies are available to compare the results**.**

## ANNEXURES

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## ABBREVATIONS USED

ACS- ACUTE CORONARY SYNDROME

STEMI- ST ELEVATION MYOCARDIAL INFARCTION.

NSTEMI- NON ST ELEVATION MYOCARDIAL INFARCTION

UA- UNSTABLE ANGINA

SHT- SYSTEMIC HYPERTENSION

DM- DIABETES MELLITUS

LVD- LEFT VENTRICULAR DYSFUNCTION

AWMI- ANTERIOR WALL MYOCARDIAL INFARCTION

IWMI- INFERIOR WALL MYOCARDIAL INFARCTION

RVMI- RIGHT VENTRICULAR MYOCARDIAL INFARCTION

CPK-MB- CREATININE PHOSPHOKINASE MB

B-BLOCKER- BETA BLOCKER

CHD- CORONARY HEART DISEASE

ACE- ANGOTENSION CONVERTING ENZYME

PCI- PERCUTANEOUS CORONARY INTREVENTION

ECG- ELECTROCARDIOGRAM

HDL-HIGH DENSUTY LIPOPROTEIN

LDL- LOW DENSITY LIPOPROTEIN

SMC- SMOOTH MUSCLE CELL

ECM- EXTRACELLULAR CELL MATRIX

UFH- UNFRACTIONATED HEPARIN

LMWH- LOW MOLECULAR WEIGHT HEPARIN

COX- CYCLOXYGENASE.

# PROFORMA

NAME:

AGE:

SEX:

ADDRESS: Op No:

D.O.A D.O.D

DURATION OF HOSPITAL STAY

HISTORY AND PAST HISTORY:

SIGNS:

GENERAL

Built: Pallor: Icterus:

Pedal oedema: Temp: Hydration:

Clubbing: PR: BP:

CVS:

RS :

PER ABDOMEN:

CNS:

INVESTIGATIONS

Complete haemogram: HB, TC,DC,ESR

RBS.

Δk-(potassium at the time of discharge – potassium at the time of admission)

Urea

Creatinine

Serum CPK-MB .

Total Cholesterol

Triglyceride level

Urine:

Sugar

Albumin

Deposits

ECG

Echocardiography

Chest X-Ray